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* * * * * * * * * * *   Welcome to STN International   * * * * * * * * * * *
* * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

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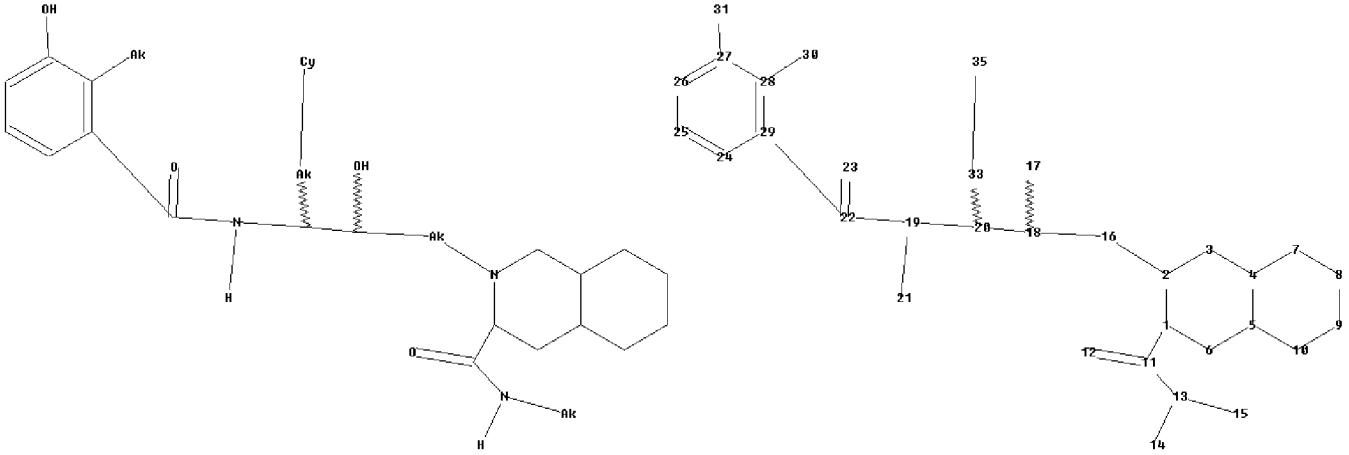


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ring nodes :
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20-33  22-23  22-29  27-31  28-30  33-35
ring bonds :
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27-28  28-29
exact/norm bonds :
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16-18  17-18  19-20  19-22  20-33  22-23  27-31  28-30  33-35
exact bonds :
1-11  13-14  18-20  19-21  22-29
normalized bonds :
24-25  24-29  25-26  26-27  27-28  28-29
isolated ring systems :
containing 1 : 24 :


G1:O,S,N

Match level :
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11:CLASS  12:CLASS  13:CLASS  14:CLASS  15:CLASS  16:CLASS  17:CLASS  18:CLASS
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=> s l1 full
L3            9 SEA SSS FUL L1

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L5            6 L3 AND PD< JULY 2003

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L5   ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2008 ACS on STN
AN   2002:964340  CAPLUS  Full-text
DN   138:39544
TI   Preparation of amino acid amides as HIV protease inhibitors
IN   Canon-Koch, Stacie S.; Alexander, Therese N.; Barvian, Mark; Bolton, Gary;
     Boyer, Fredrick E.; Burke, Benjamin J.; Holler, Tod; Jewell, Tanya M.;
     Prasad, Josyula Vara; Kucera, David J.; Linton, Maria A.; Machak, Jeff;
     Mitchell, Lennert J.; Murphy, Sean T.; Reich, Siegfried H.; Skalitzky,
     Donald J.; Tatlock, John H.; Varney, Michael D.; Virgil, Scott C.; Webber,
     Stephen E.; Worland, Stephen T.; Melnick, Michael
PA   Agouron Pharmaceuticals, Inc., USA
SO   PCT Int. Appl., 306 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 4
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     ZA 2003009040        A     20050527    ZA 2003-9040           20031120
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     MX 2003PA11397       A     20050307    MX 2003-PA11397        20031209
     AU 2006235964        A1    20061130    AU 2006-235964         20061110
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OS MARPAT 138:39544

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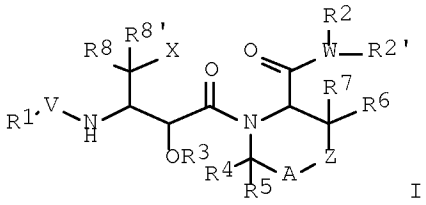

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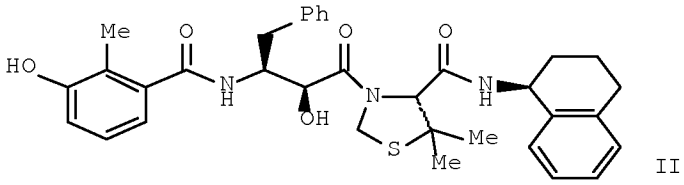


II

AB Synthetic amides I [R1 is an aliphatic, carbo- or heterocyclic group, OR1', SR1', NHR1', NR1'R1'', or COR1', where R1' is an aliphatic, carbo- or heterocyclic group and R1'' is H or an aliphatic group or NR1'R1" is (un)substituted heterocyclyl; V is CO, CS, or SO2; R2 is an aliphatic, carbocyclic, or carbocyclic aliphatic group, or NR2aR2b, where R2a is an aliphatic, carbo-, or heterocyclic group and R2b is H or an aliphatic group; W is N, O, C, or CH; R2' is H or an aliphatic group (when W is N, C or CH) or R2R2'W is an (un)substituted carbo- or heterocyclic ring; R2 is absent when W is O; X is (un)substituted Ph, phenoxy, phenylthio, benzyl, or phenethyl; R8, R8' are H, halo, or an aliphatic group; A is CH2, CHRA, or is absent; Z is S, O, SO, SO2, CH2, CHF, CF2, CHOH, CH(ORZ), CH(NRZRZ'),CH(SRZ), CO, or CHRZ, where RZ is an aliphatic, carbo-, or heterocyclic group and RZ' is H or an aliphatic group; or RA and RZ taken together with A and Z form an (un)substituted carbo- or heterocyclic ring; R3 is H or an aliphatic group; R4, R5 are H, halo, an aliphatic or acyl group group; R4 may combine with R5 or with R6 or R7 to form a ring; R6, R7 are H or an aliphatic group] inhibit or block the biol. activity of the HIV protease. Thus, thiazolidinecarboxamide derivative II was prepared via amidation reactions and showed Ki = 0.21 nM for inhibition of HIV-1 protease. A combinatorial chemical approach to HIV protease inhibitors was also presented.

IT 478698-82-7P 478699-77-3P

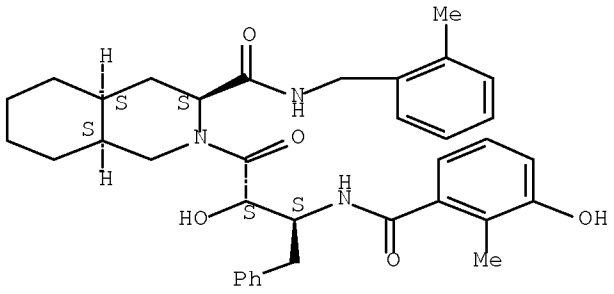
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino acid amides as HIV protease inhibitors)

RN 478698-82-7 CAPLUS

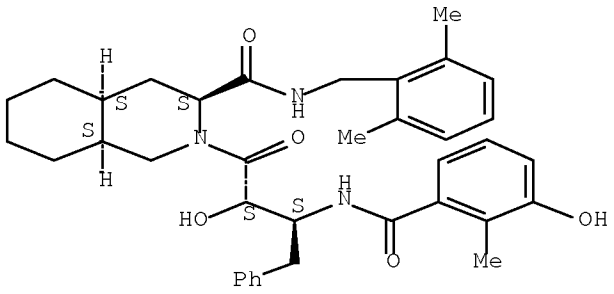
CN 3-Isoquinolinecarboxamide, decahydro-2-[(2S,3S)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-1-oxo-4-phenylbutyl]-N-[(2-methylphenyl)methyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



RN 478699-77-3 CAPLUS
CN 3-Isoquinolinecarboxamide, N-[(2,6-dimethylphenyl)methyl]decahydro-2-[(2S,3S)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-1-oxo-4-phenylbutyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1998:351758 CAPLUS Full-text
DN 129:45325
TI Liquid pharmaceutical compositions containing HIV protease inhibitors
IN Lipari, John; Al-Razzak, Laman A.; Ghosh, Soumojeet; Gao, Rong; Kaul, Dilip
PA Abbott Laboratories, USA
SO PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9822106	A1	19980528	WO 1997-US20794	19971112 <--

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RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,

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	CA 2271196	C	19980528	CA 1997-2271196	19971112 <--
	CA 2271196	A1	19980528		
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	AU 717546	B2	20000330		
	EP 942721	A1	19990922	EP 1997-947510	19971112 <--
	EP 942721	B1	20030122		
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	JP 2000515555	T	20001121	JP 1998-523751	19971112 <--
	JP 3592337	B2	20041124		
	HU 2000002932	A2	20010129	HU 2000-2932	19971112 <--
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	EP 1283041	A1	20030212	EP 2002-11533	19971112 <--
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	PT 942721	T	20030630	PT 1997-947510	19971112 <--
	IL 129300	A	20030706	IL 1997-129300	19971112
	ES 2191862	T3	20030916	ES 1997-947510	19971112
	PL 190185	B1	20051130	PL 1997-336980	19971112
	SK 285022	B6	20060406	SK 1999-655	19971112
	CN 1989963	A	20070704	CN 2005-10128757	19971112
	CN 101103984	A	20080116	CN 2006-10101904	19971112
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	HK 1022441	A1	20031031	HK 2000-101651	20000317
	AU 757970	B2	20030313	AU 2000-39414	20000609 <--
	JP 2004346077	A	20041209	JP 2004-163024	20040601
PRAI	US 1996-754390	A	19961121		
	AU 1998-52573	A3	19971112		
	CA 1997-2271196	A3	19971112		
	CN 1997-199780	A3	19971112		
	CN 2008-10128757	A3	19971112		
	EP 1997-947510	A3	19971112		
	JP 1998-523751	A3	19971112		
	WO 1997-US20794	W	19971112		

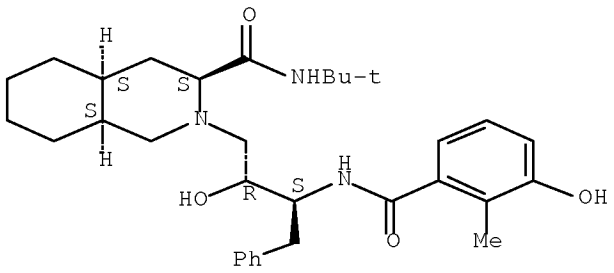
AB A liquid pharmaceutical composition providing improved oral bioavailability is disclosed for compds. which are inhibitors of HIV protease. In particular, the composition comprises a solution in a pharmaceutically acceptable organic solvent of (a) the HIV protease inhibitor and optionally, (b) a surfactant. The composition can optionally be encapsulated in either hard gelating capsules or soft elastic capsules (SEC). A capsule composition was prepared containing ritonavir 20, ethanol 10, oleic acid 69.99, and BHT 0.01% by weight

IT 168898-57-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(liquid pharmaceutical compns. containing HIV protease inhibitors)

RN 168898-57-5 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3S)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-phenylbutyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1997:720276 CAPLUS Full-text
DN 127:302916
TI Viracept (Nelfinavir Mesylate, AG1343): A Potent, Orally Bioavailable Inhibitor of HIV-1 Protease
AU Kaldor, Stephen W.; Kalish, Vincent J.; Davies, Jay F. ,II; Shetty, Bhasker V.; Fritz, James E.; Appelt, Krzysztof; Burgess, Jeffrey A.; Campanale, Kristina M.; Chirgadze, Nickolay Y.; Clawson, David K.; Dressman, Bruce A.; Hatch, Steven D.; Khalil, Deborah A.; Kosa, Maha B.; Lubbehusen, Penny P.; Muesing, Mark A.; Patick, Amy K.; Reich, Siegfried H.; Su, Kenneth S.; Tatlock, John H.
CS Agouron Pharmaceuticals Inc., San Diego, CA, 92121, USA
SO Journal of Medicinal Chemistry (1997), 40(24), 3979-3985
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB Using a combination of iterative structure-based design and an anal. of oral pharmacokinetics and antiviral activity, AG1343 (Viracept, nelfinavir mesylate), a nonpeptidic inhibitor of HIV-1 protease, was identified. AG1343 is a potent enzyme inhibitor (Ki = 2 nM) and antiviral agent (HIV-1 ED50 = 14 nM). An X-ray cocrystal structure of the enzyme-AG1343 complex reveals how the novel thiophenyl ether and phenol-amide substituents of the inhibitor interact with the S1 and S2 subsites of HIV-1 protease, resp. In vivo studies indicate that AG1343 is well absorbed orally in a variety of species and possesses favorable pharmacokinetic properties in humans. AG1343 (Viracept) has recently been approved for marketing for the treatment of AIDS.
IT 169104-89-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of and HIV-1 protease inhibition by viracept and analogs)
RN 169104-89-6 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-phenylbutyl]-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]-, monomethanesulfonate (salt) (9CI) (CA INDEX NAME)

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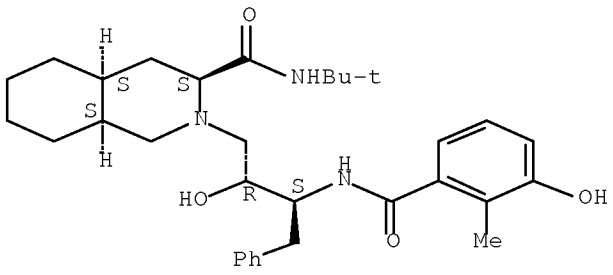
CRN 168898-57-5

CMF C32 H45 N3 O4

Absolute stereochemistry. Rotation (-).



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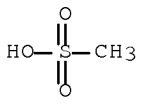
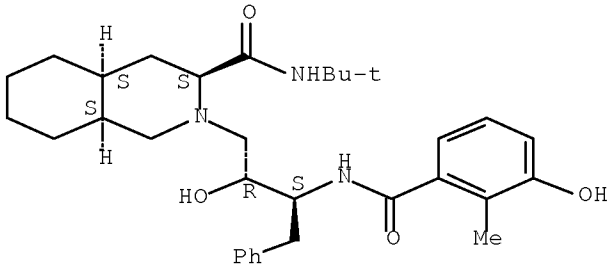


IT 168898-57-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of and HIV-1 protease inhibition by viracept and analogs)
RN 168898-57-5 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3S)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-phenylbutyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1996:106715 CAPLUS Full-text

DN 124:317888
TI Aromatic and heterocyclic amides as HIV protease inhibitors
IN Dressman, Bruce A.; Fritz, James E.; Hammond, Marlys; Hornback, William J.; Kaldor, Stephen W.; Kalish, Vincent J.; Munroe, John E.; Reich, Siegfried H.; Tatlock, John H.; et al.
PA Agouron Pharmaceuticals, Inc., USA
SO U.S., 78 pp. Cont.-in-part of U.S. Ser. No. 133,543, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

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	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
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	PT 889036	T	20050531	PT 1998-113006	19941007
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	AT 362918	T	20070615	AT 2003-11749	19941007
	ES 2287387	T3	20071216	ES 2003-11749	19941007

	IL 125098	A	20000131	IL 1994-125098	19941031 <--
	IL 111472	A	20000601	IL 1994-111472	19941031 <--
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	US 5827891	A	19981027	US 1995-478599	19950607 <--
	US 5827859	A	19981027	US 1995-478934	19950607 <--
	US 5834467	A	19981110	US 1995-482504	19950607 <--
	US 5837710	A	19981117	US 1995-479765	19950607 <--
	US 5846993	A	19981208	US 1995-481833	19950607 <--
	US 5852043	A	19981222	US 1995-484706	19950607 <--
	US 5859002	A	19990112	US 1995-474138	19950607 <--
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	US 20020077338	A1	20020620	US 2001-885056	20010621 <--
	US 6525215	B2	20030225		
	US 20030216569	A1	20031120	US 2002-300638	20021121
	US 6693199	B2	20040217		
	HK 1056172	A1	20071012	HK 2003-108464	20031120
PRAI	US 1993-133543	B2	19931007		
	US 1993-133696	B2	19931007		
	US 1992-995621	B2	19921222		
	US 1993-137254	B2	19931018		
	US 1994-190764	A	19940202		
	CA 1994-2173328	A3	19941007		
	EP 1994-930609	A3	19941007		
	EP 1998-113006	A3	19941007		
	JP 1995-511006	A3	19941007		
	WO 1994-US11307	W	19941007		
	IL 1994-111472	A3	19941031		
	US 1995-481831	A1	19950607		
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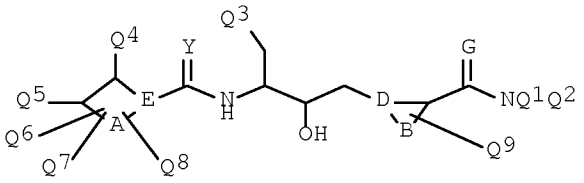
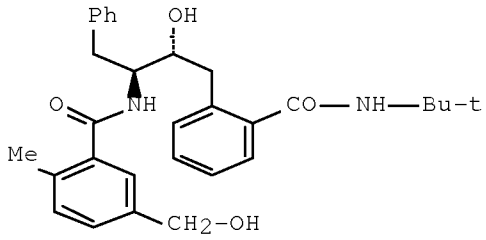
OS	MARPAT 124:317888				
GI					



I



II

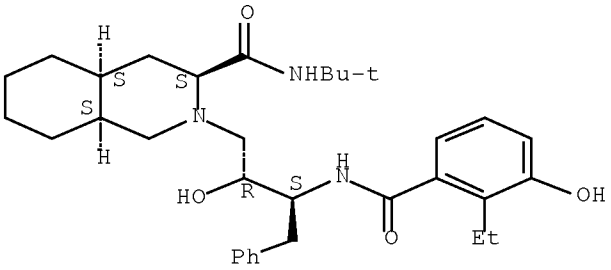
AB HIV protease inhibitors I wherein: Q1 and Q2 are independently H, (un)substituted alkyl and aryl, and Q1 and Q2 may form a ring with G; Q3 = e.g., mercapto, (un)substituted alkoxy, aryloxy, thioether, amino, heterocycle, aryl; Q4-Q8 are independently, e.g., H, OH, mercapto, nitro, halo; Y and G are independently O, NH, N-alkyl, S, Se, two H atoms; D is C or N; E is C or N; Q9 = e.g., H, halo, OH, mercapto; the A and B rings are carbocyclic or heterocyclic; obtainable by chemical synthesis, inhibit or block the biol. activity of the HIV protease enzyme, causing the replication of the HIV virus to terminate. These compds., as well as pharmaceutical compns. that contain these compds. and optionally other anti-viral agents as active ingredients, are suitable for treating patients or hosts infected with the HIV virus, which is known to cause AIDS. Thus, e.g., amide coupling of [2R-(2R*,3S*)]-N-t-butyl-2-(3-amino-2- hydroxy-4-phenylbutyl)benzamide (preparation given) with 2-methyl-5- hydroxymethyl benzoic acid (preparation given) afforded [2'R-(2'R*,3'S*)]-N-t- butyl-2-[2'-hydroxy-3'-phenylmethyl-4'-aza-5'-oxo-5'-(2"-methyl-5"- hydroxymethylphenyl)pentyl]benzamide (II) which inhibited HIV-1 protease in the fluorescence assay with IC50 = 0.006 μg/mL. Pharmaceutical formulations were given.

IT 168898-48-4P 168898-57-5P 168898-65-5P
168898-66-6P 168898-67-7P 169104-88-5P
169104-89-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aromatic and heterocyclic amides as HIV protease inhibitors)

RN 168898-48-4 CAPLUS

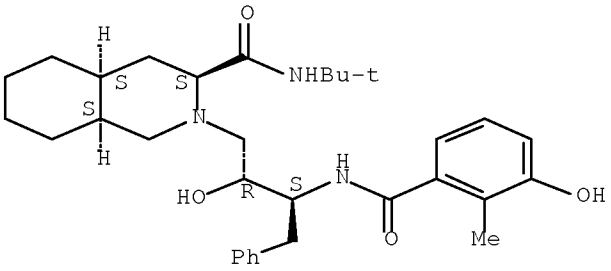
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)-2-[3-[(2-ethyl-3-hydroxybenzoyl)amino]-2-hydroxy-4-phenylbutyl]decahydro-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



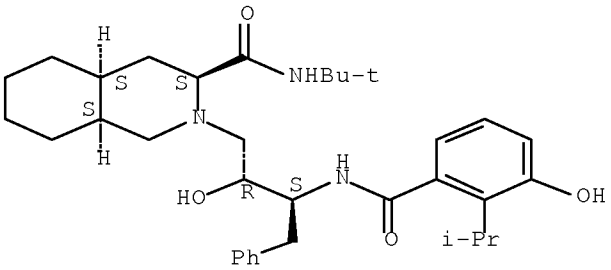
RN 168898-57-5 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3S)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-phenylbutyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



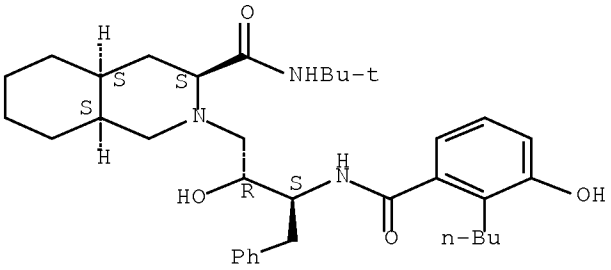
RN 168898-65-5 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[2-hydroxy-3-[[3-hydroxy-2-(1-methylethyl)benzoyl]amino]-4-phenylbutyl]-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



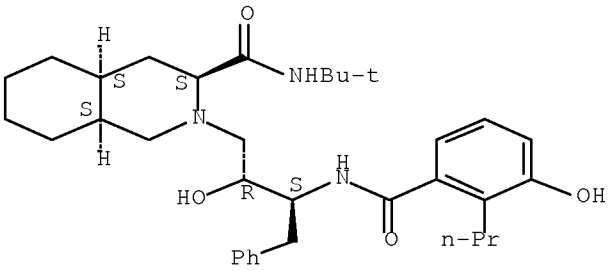
RN 168898-66-6 CAPLUS
CN 3-Isoquinolinecarboxamide, 2-[3-[(2-butyl-3-hydroxybenzoyl)amino]-2-hydroxy-4-phenylbutyl]-N-(1,1-dimethylethyl)decahydro-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 168898-67-7 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[2-hydroxy-3-[(3-hydroxy-2-propylbenzoyl)amino]-4-phenylbutyl]-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

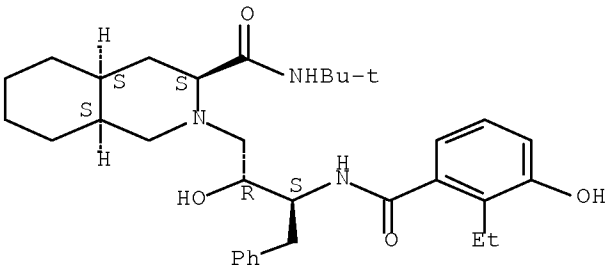


RN 169104-88-5 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)-2-[3-[(2-ethyl-3-hydroxybenzoyl)amino]-2-hydroxy-4-phenylbutyl]decahydro-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]-, monomethanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

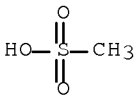
CRN 168898-48-4
CMF C33 H47 N3 O4

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-75-2
CMF C H4 O3 S

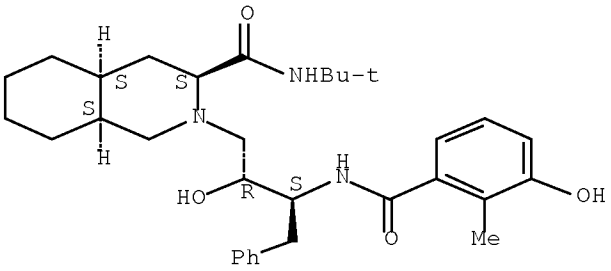


RN 169104-89-6 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-phenylbutyl]-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]-, monomethanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

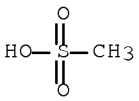
CRN 168898-57-5
CMF C32 H45 N3 O4

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-75-2
CMF C H4 O3 S



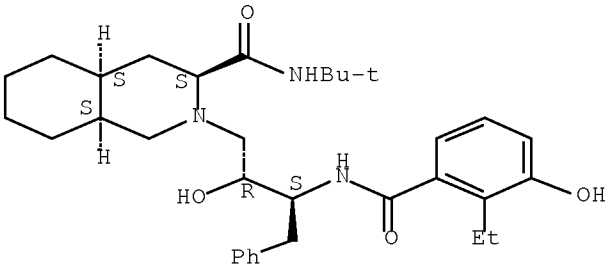
L5 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1995:994185 CAPLUS Full-text
DN 124:87033
TI Preparation of HIV protease inhibitors and their (aminohydroxyalkyl)piperazine intermediates.
IN Jungheim, Louis Nickolaus; Shepherd, Timothy Alan
PA Eli Lilly and Co., USA

SO PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9521164	A1	19950810	WO 1994-US11352	19941006 <--
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5461154	A	19951024	US 1994-190630	19940202 <--
CA 2180860	A1	19950810	CA 1994-2180860	19941006 <--
AU 9479304	A	19950821	AU 1994-79304	19941006 <--
EP 741719	A1	19961113	EP 1994-930064	19941006 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
HU 76285	A2	19970728	HU 1996-2105	19941006 <--
BR 9408530	A	19970805	BR 1994-8530	19941006 <--
JP 09509657	T	19970930	JP 1994-520584	19941006 <--
PRAI US 1994-190630	A	19940202		
WO 1994-US11352	W	19941006		

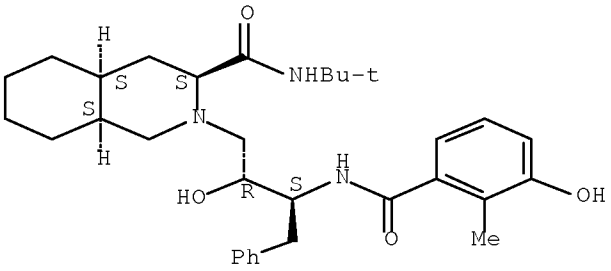
OS MARPAT 124:87033
GI For diagram(s), see printed CA Issue.
AB Intermediates [I; R = alkyl, pyridylmethyl; R1 = aryl, arylthio; R3 = CON(R4)2, Q1, Q2; p = 4, 5; R4 = H, alkyl, hydroxyalkyl; R5, R6 = H, OH, alkyl, alkoxy, hydroxyalkyl], were prepared by (a) reduction of pyrazines (II) to give piperazines, (b) alkylation of the piperazines to give intermediates (III), (c) alkylation of III with (IV; R11 = protecting group), and (d) optional deprotection. Thus, pyrazine-2-carboxylic acid in DMF/THF was treated with carbonyldiimidazole and then with Me3CNH2 to give 95% pyrazine 2-N-tert-butylcarboxamide. The latter in EtOH was hydrogenated at 60 psi and 40° overnight to give 95% piperazine 2-N-tert-butylcarboxamide. This in H2O/MeCN was treated with K2CO3 and 3-chloromethylpyridine hydrochloride overnight to give 18% 4-(pyrid-3-ylmethyl)piperazine 2-N-tert-butylcarboxamide. Reflux of the latter compound with [1S-(1R*,1'R*)]-1-[(1'-N-benzyloxycarbonylamino-2'- phenyl)ethyl]oxirane in Me2CHOH gave 26% [2S-(2R*,2S*,3'R*)]-1-[2'-hydroxy- 3'-(N-benzyloxycarbonylamino)-4'-phenylbutyl]-4-(pyrid-3''- ylmethyl)piperazine 2-N-tert-butylcarboxamide. [3S-(3R*,8aR*,2'S*,3'S*)]- 2-[2'-hydroxy-3'-phenylthiomethyl-4'-aza-5'-(2''-methyl-3''- hydroxyphenyl)pentyl]decahydroisoquinoline 3-N-tert-butylcarboxamide (preparation given) inhibited HIV-1 protease with a normalized IC50 = 0.25 ng/mL.
IT 168898-48-4P 168898-57-5P 168898-65-5P
168898-66-6P 168898-67-7P 169104-88-5P
169104-89-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of HIV protease inhibitors and their (aminohydroxyalkyl)piperazine intermediates)
RN 168898-48-4 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)-2-[3-[(2-ethyl-3-hydroxybenzoyl)amino]-2-hydroxy-4-phenylbutyl]decahydro-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



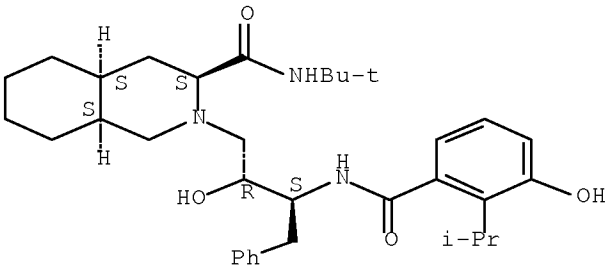
RN 168898-57-5 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3S)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-phenylbutyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



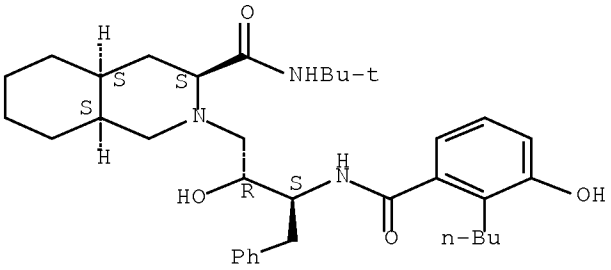
RN 168898-65-5 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[2-hydroxy-3-[[3-hydroxy-2-(1-methylethyl)benzoyl]amino]-4-phenylbutyl]-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



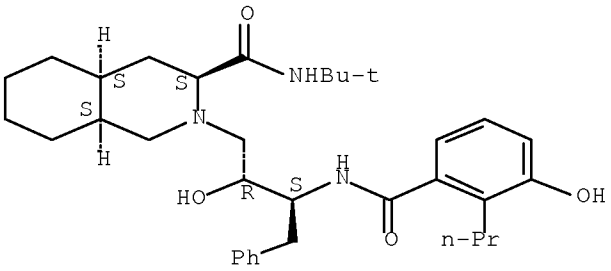
RN 168898-66-6 CAPLUS
CN 3-Isoquinolinecarboxamide, 2-[3-[(2-butyl-3-hydroxybenzoyl)amino]-2-hydroxy-4-phenylbutyl]-N-(1,1-dimethylethyl)decahydro-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 168898-67-7 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[2-hydroxy-3-[(3-hydroxy-2-propylbenzoyl)amino]-4-phenylbutyl]-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

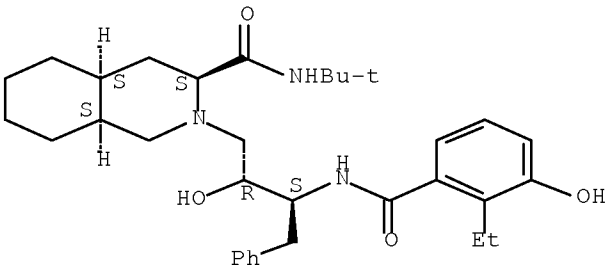


RN 169104-88-5 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)-2-[3-[(2-ethyl-3-hydroxybenzoyl)amino]-2-hydroxy-4-phenylbutyl]decahydro-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]-, monomethanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

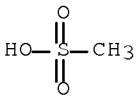
CRN 168898-48-4
CMF C33 H47 N3 O4

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-75-2
CMF C H4 O3 S

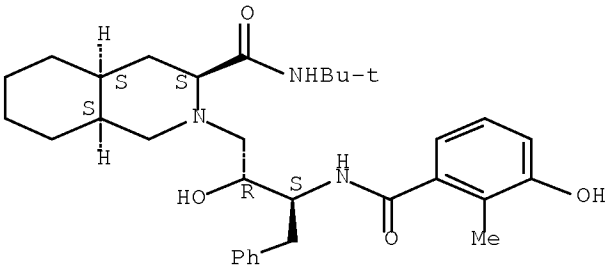


RN 169104-89-6 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-phenylbutyl]-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]-, monomethanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

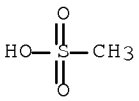
CRN 168898-57-5
CMF C32 H45 N3 O4

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-75-2
CMF C H4 O3 S



L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1995:851692 CAPLUS Full-text
DN 123:256539
TI Preparation of arylheterocyclyl compounds as HIV protease inhibitors
IN Dressman, Bruce A.; Fritz, James E.; Hammond, Marlys; Hornback, William J.; Kaldor, Stephen W.; Kalish, Vincent J.; Munroe, John E.; Reich, Siegfried Heinz; Tatlock, John H.; et al.

PA Agouron Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 343 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9509843	A1	19950413	WO 1994-US11307	19941007 <--
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	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
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	ZA 9407815	A	19960708	ZA 1994-7815	19941006 <--
	AU 9479674	A	19950501	AU 1994-79674	19941007 <--
	AU 694746	B2	19980730		
	EP 722439	A1	19960724	EP 1994-930609	19941007 <--
	EP 722439	B1	20020814		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
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	PL 185647	B1	20030630	PL 1994-313871	19941007 <--
	RO 119363	B1	20040830	RO 1996-738	19941007
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	NO 9601382	A	19960409	NO 1996-1382	19960403 <--
	NO 307050	B1	20000131		
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PRAI	US 1993-133543	A	19931007		
	US 1993-133696	A	19931007		
	US 1994-190764	A	19940202		
	WO 1994-US11307	W	19941007		

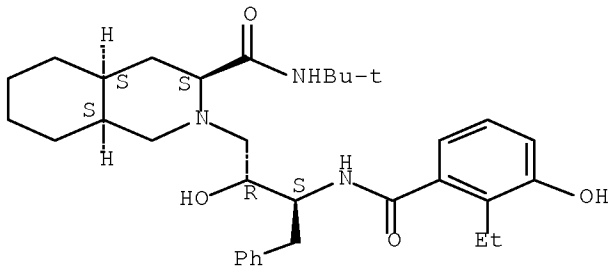
OS CASREACT 123:256539; MARPAT 123:256539
GI For diagram(s), see printed CA Issue.
AB Title compds I (Q1, Q2 = H, alkyl, aryl optionally substituted, Q1 and Q2 may form a ring with G; Q3 = HS, alkoxy, aryloxy, thioether, amino, alkyl, cycloalkyl all optionally substituted, saturated and partially saturated heterocyclyl; Q4-8 = H, HO, HS, O2N, halo, etc.; Y, G = O, HN, alkyl-N, S, Se, 2H; D, E = C, N, etc.; Q9 = H, halo, HO, HS, etc.; A, B = (substituted) carbocyclyl or heterocyclyl) or a salt thereof, are prepared To [3S-(3R,4aR,8aR,2'S,3'R)]-2-[3'-amino-2-hydroxy-4'-phenyl]butyldecahydroisoquinoline-3-N-tert-butylcarboxamide (preparation given), 2-fluoro-3-hydroxybenzoic acid (preparation given) and 1-hydroxybenzotriazole in THF was added 1,3-dicyclohenxylcarbodiimide to give the title compound [3S-(3R,4aR,8aR,2'S,3'R)]-2-[2'-hydroxy-3'- phenylmethyl-4'-aza-5'-oxo-5'-(2"-fluoro-3"-hydroxyphenyl)pentyl]decahydro isoquinoline-3-N-tert-butylcarboxamide. HIV protease inhibition was demonstrated with I. Pharmaceutical formulations comprising I are given.
IT 168898-48-4P 168898-57-5P 168898-65-5P
168898-66-6P 168898-67-7P 169104-88-5P
169104-89-6P

RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arylheterocyclyl compds. as HIV protease inhibitors)

RN 168898-48-4 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)-2-[3-[(2-ethyl-3-hydroxybenzoyl)amino]-2-hydroxy-4-phenylbutyl]decahydro-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]- (9CI) (CA INDEX NAME)

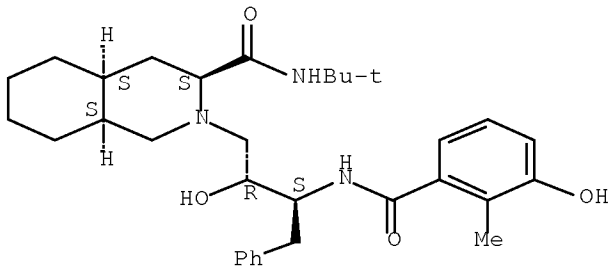
Absolute stereochemistry. Rotation (-).



RN 168898-57-5 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3S)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-phenylbutyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

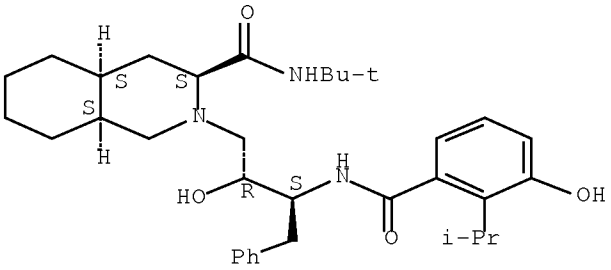
Absolute stereochemistry. Rotation (-).



RN 168898-65-5 CAPLUS

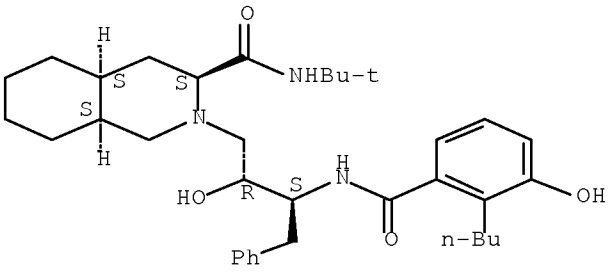
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[2-hydroxy-3-[[3-hydroxy-2-(1-methylethyl)benzoyl]amino]-4-phenylbutyl]-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



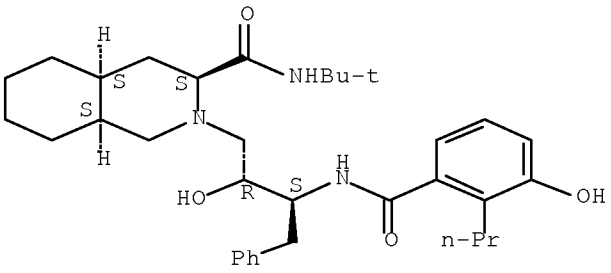
RN 168898-66-6 CAPLUS
CN 3-Isoquinolinecarboxamide, 2-[3-[(2-butyl-3-hydroxybenzoyl)amino]-2-hydroxy-4-phenylbutyl]-N-(1,1-dimethylethyl)decahydro-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 168898-67-7 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[2-hydroxy-3-[(3-hydroxy-2-propylbenzoyl)amino]-4-phenylbutyl]-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

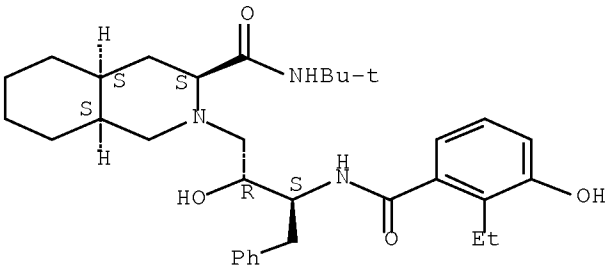


RN 169104-88-5 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)-2-[3-[(2-ethyl-3-hydroxybenzoyl)amino]-2-hydroxy-4-phenylbutyl]decahydro-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]-, monomethanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

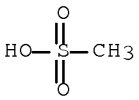
CRN 168898-48-4
CMF C33 H47 N3 O4

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-75-2
CMF C H4 O3 S

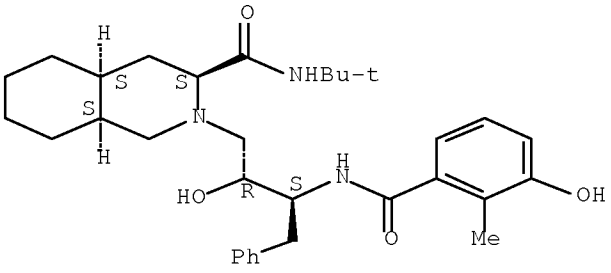


RN 169104-89-6 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-phenylbutyl]-, [3S-[2(2S*,3R*),3α,4aβ,8aβ]]-, monomethanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

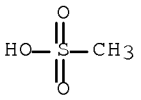
CRN 168898-57-5
CMF C32 H45 N3 O4

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-75-2
CMF C H4 O3 S



=> s l4 not l5
L6 1 L4 NOT L5

=> dis l6 bib abs fhitstr

L6 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:857219 CAPLUS Full-text
DN 141:314632
TI Preparation of amino acid amides as HIV protease inhibitors
IN Kucera, David John; Scott, Robert William
PA Agouron Pharmaceuticals, Inc., USA
SO U.S. Pat. Appl. Publ., 296 pp., Cont.-in-part of U.S. Ser. No. 166,979.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

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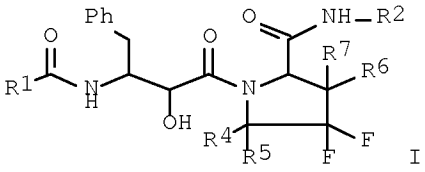
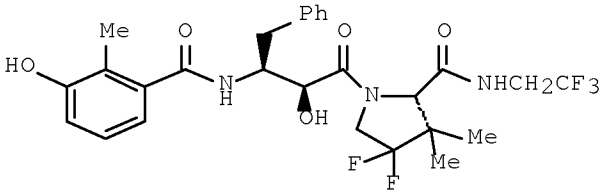
PI	US 20040204591	A1	20041014	US 2003-729645	20031204
	US 7094909	B2	20060822		
	US 20030225071	A1	20031204	US 2002-166979	20020611
	US 7179918	B2	20070220		
	EP 1739082	A1	20070103	EP 2006-20180	20020611
	R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR, AL, LT, LV, MK, RO, SI				
	ZA 2003009041	A	20040722	ZA 2003-9041	20031120
	ZA 2003009040	A	20050527	ZA 2003-9040	20031120
	US 20070021354	A1	20070125	US 2006-450943	20060609
	AU 2006235964	A1	20061130	AU 2006-235964	20061110
PRAI	US 2001-297460P	P	20010611		
	US 2001-297729P	P	20010611		
	US 2002-166979	A2	20020611		
	AU 2002-345644	A3	20020611		
	EP 2002-744295	A3	20020611		

OS MARPAT 141:314632
GI



I



II

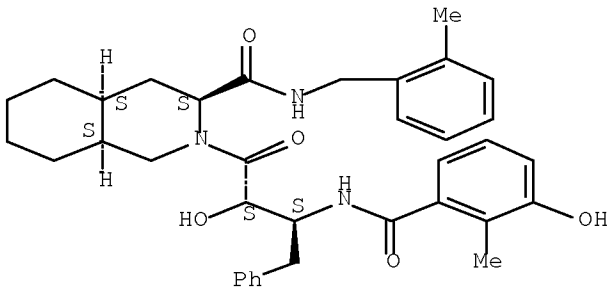
AB Synthetic amides I [R1 is a 5- or 6-membered monocyclic carbo- or heterocyclic ring which is optionally substituted by alkyl, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy or heteroarylcarbonyloxy; R2 is haloalkyl; R4-R7 are H or alkyl] or their pharmaceutically-active salts, metabolites or prodrugs are useful as inhibitors of the HIV protease enzyme. Thus, pyrrolidinecarboxamide derivative II was prepared via amidation reactions. A combinatorial chemical approach to HIV protease inhibitors was also presented.

IT 478698-82-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid amides as HIV protease inhibitors)

RN 478698-82-7 CAPLUS

CN 3-Isoquinolinecarboxamide, decahydro-2-[(2S,3S)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-1-oxo-4-phenylbutyl]-N-[(2-methylphenyl)methyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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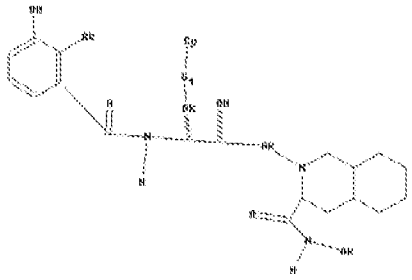

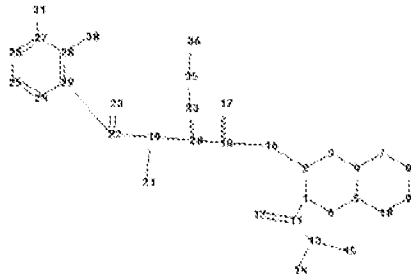

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ring nodes :
1  2  3  4  5  6  7  8  9  10  24  25  26  27  28  29
chain bonds :
1-11  2-16  11-12  11-13  13-14  13-15  16-18  17-18  18-20  19-20  19-21  19-22
20-33  22-23  22-29  27-31  28-30  33-35  35-36
ring bonds :
1-2  1-6  2-3  3-4  4-5  4-7  5-6  5-10  7-8  8-9  9-10  24-25  24-29  25-26  26-27
27-28  28-29
exact/norm bonds :
1-2  1-6  2-3  2-16  3-4  4-5  4-7  5-6  5-10  7-8  8-9  9-10  11-12  11-13  13-15
16-18  17-18  19-20  19-22  20-33  22-23  27-31  28-30  33-35  35-36
exact bonds :
1-11  13-14  18-20  19-21  22-29
normalized bonds :
24-25  24-29  25-26  26-27  27-28  28-29
isolated ring systems :
containing 1 : 24 :


G1:O,S,N

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:CLASS  12:CLASS  13:CLASS  14:CLASS  15:CLASS  16:CLASS  17:CLASS  18:CLASS
19:CLASS  20:CLASS  21:CLASS  22:CLASS  23:CLASS  24:Atom  25:Atom  26:Atom
27:Atom  28:Atom  29:Atom  30:CLASS  31:CLASS  33:CLASS  35:CLASS  36:Atom



=> s l7 sam
L8            2 SEA SSS SAM L7

=> s l7 full
L9           33 SEA SSS FUL L7

=> file caplus

=> s l9
L10       2032 L9

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      23779907 PD< JULY 2003
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L11       1028 L10 AND PD< JULY 2003

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L12          0 L11 AND ANTICORONAVIRUS

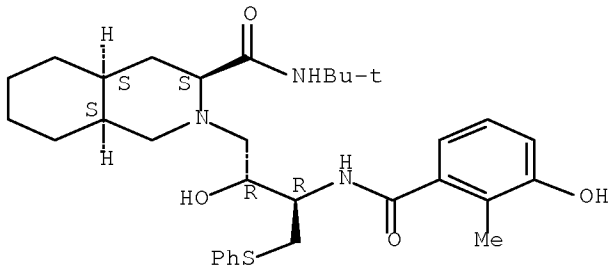
=> s l11 and sars
          4507 SARS
L13          0 L11 AND SARS

=>  s l11 and coroavirus
             1 COROAVIRUS
L14          0 L11 AND COROAVIRUS
=> dis l11 500-525 bib abs hitstr

L11  ANSWER 500 OF 1028  CAPLUS  COPYRIGHT 2008 ACS on STN
AN   2001:861052  CAPLUS  Full-text
DN   136:193703
TI   Effect of combination therapy including protease inhibitors on mortality
     among children and adolescents infected with HIV-1
AU   Gortmaker, Steven L.; Hughes, Michael; Cervia, Joseph; Brady, Michael;
     Johnson, George M.; Seage, George R., III; Song, Lin Ye; Dankner, Wayne
     M.; Oleske, James M.
CS   Pediatric AIDS Clinical Trials Group Protocol 219 Team, Center
     Biostatistics AIDS Res., Harvard Sch. Public Health, Boston, MA, USA
SO   New England Journal of Medicine (2001), 345(21), 1522-1528
     CODEN: NEJMAG; ISSN: 0028-4793
PB   Massachusetts Medical Society
DT   Journal
LA   English
AB    Combination therapy including protease inhibitors has been shown to be
      effective in treating adults infected with human immunodeficiency virus type 1
      (HIV-1), but there are only limited data regarding the treatment of children
      and adolescents.  A cohort of 1028 HIV-1-infected children and adolescents,
      from birth through 20 yr of age, who were enrolled in research clinics in the
      United States before 1996 was followed prospectively through 1999.  We used
      proportional-hazards regression models to estimate the effect on mortality of
      combination therapy including protease inhibitors.  Seven percent of the
      subjects were receiving combination therapy including protease inhibitors in
      1996; by 1999, 73 % were receiving such therapy.  In univariate analyses, a
      higher base-line percentage of lymphocytes that were CD4-pos., a higher weight
      for age, a higher height for age, black race, Hispanic ethnic background,
      younger age, and perinatally acquired infection were associated with a longer
      median time to the initiation of this type of therapy (P<0.001).  After
      adjustment for covariates, the differences among racial and ethnic groups in
      the time to initiation were not statistically significant.  Mortality declined
      from 5.3% in 1996 to 2.1% in 1997; 0.9% in 1998, and 0.7% in 1999 (P for trend
      <0.001).  There were redns. in mortality in all sub-groups defined according
      to age, sex, percentage of CD4+ lymphocytes, educational level of the parent
      or guardian, and race or ethnic background.  In adjusted analyses, the
      initiation of combination therapy including protease inhibitors was
      independently associated with reduced mortality (hazard ratio for death, 0.33;
      95 % confidence interval, 0.19 to 0.58; P<0.001).  The use of combination
      therapy including protease inhibitors has markedly reduced mortality among
      children and adolescents infected with HIV-1.
IT   159989-64-7, Nelfinavir
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (effect of combination therapy including protease inhibitors on
```

mortality among human children and adolescents infected with HIV-1)
RN 159989-64-7 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.

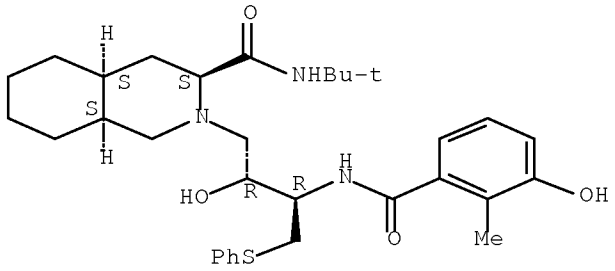


RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 501 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:845561 CAPLUS Full-text
DN 136:337596
TI Genotypic and phenotypic evidence of different drug-resistance mutation patterns between B and non-B subtype isolates of human immunodeficiency virus type 1 found in Brazilian patients failing HAART
AU Caride, Elena; Hertogs, Kurt; Larder, Brendan; Dehertogh, Pascale; Brindeiro, Rodrigo; Machado, Elizabeth; De Sa, Carlos A. M.; Eyer-Silva, Walter A.; Sion, Fernando Samuel; Passioni, Luiz F. C.; Menezes, Jaqueline A.; Calazans, Alexandre R.; Tanuri, Amilcar
CS Laboratory of Molecular Virology, Genetic Department, UFRJ, Rio de Janeiro, CEP: 21944-970, Brazil
SO Virus Genes (2001), 23(2), 193-202
CODEN: VIGEET; ISSN: 0920-8569
PB Kluwer Academic Publishers
DT Journal
LA English
AB We have investigated the phenotypic and genotypic susceptibility of 14 HIV-1 strains isolated from individuals failing HAART therapy to protease inhibitors (PI). Proviral and plasma viral pol gene fragment were amplified, sequenced and subtyped. Nine samples clustered with protease subtype B reference strains and the remaining samples were classified as non-B subtype corresponding to subtype F (n=4) and subtype A (n=1). Although all patients were treated with similar PI drug regimen, the non-B subtype isolates did not present the L90M and 184V mutations and used mainly G48V and V82A/F to achieve drug resistance. A strong crossresistance phenotype among all four PI was associated with the mutation L90M in the subtype-B isolates, and with G48V and V82A/F in the non-B counterparts. This observation revealed that the non-B viruses tested had specific genotypic characteristics contrasting with the subtype-B isolates.
IT 159989-64-7, Nelfinavir
RL: PAC (Pharmacological activity); BIOL (Biological study)
(genotypic and phenotypic evidence of different drug-resistance mutation patterns between B and non-B subtype isolates of HIV-1 found in Brazilian patients failing HAART)
RN 159989-64-7 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.

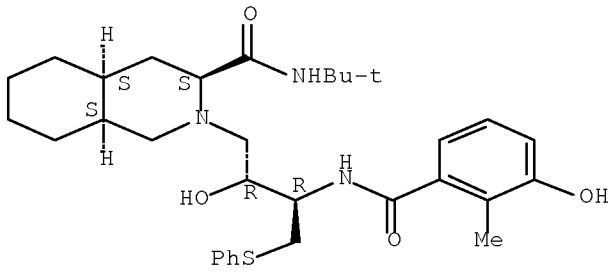


RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 502 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:841654 CAPLUS Full-text
DN 136:144718
TI Improvement of HAART-associated insulin resistance and dyslipidemia after replacement of protease inhibitors with abacavir
AU Walli, R.; Michl, G. M.; Bogner, J. R.; Goebel, F. D.
CS Medizinische Poliklinik, Universitat Munchen, Munchen, Germany
SO European Journal of Medical Research (2001), 6(10), 413-421
CODEN: EJMRFL; ISSN: 0949-2321
PB I. Holzapfel Publishers
DT Journal
LA English
AB Objective: To assess the effect of replacing protease inhibitors (PIs) with abacavir on insulin sensitivity and plasma lipids. Design: Pilot study including 31 patients with sustained virol. control on their first PI-containing HAART regimen. 16 Patients were switched from PIs to abacavir (ABC group), 15 patients continued on PIs (PI group). In all patients, nucleoside-analog reverse transcriptase inhibitors were continued. Methods: Insulin sensitivity (using an i.v. insulin tolerance test) and fasting total cholesterol and triglycerides were determined at baseline, month 3, 6, 9 and 12. Results: In the ABC group, there was a significant increase in median insulin sensitivity from baseline within 6 mo (+49 μmol/l/min), and a significant decrease in both triglycerides (-41 mg/dL) and cholesterol (-40 mg/dL) at month 3. These changes were sustained through month 12. In addition, a reversal of baseline insulin resistance, hypercholesterolemia and hypertriglyceridemia was observed in the majority of patients. In the PI group, no significant changes in insulin sensitivity, triglycerides and cholesterol were observed There was a significant correlation between the changes in insulin sensitivity, triglycerides and cholesterol. Interpretation: Switching from PIs to abacavir is associated with an improvement of insulin sensitivity and a decrease of cholesterol and triglycerides in the majority of patients with HAART-associated metabolic alterations and therefore might be an alternative for patients to PI-containing HAART regimens.
IT 159989-64-7, Nelfinavir
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(improvement of HAART-associated insulin resistance and dyslipidemia after

replacement of protease inhibitors with abacavir in humans)
RN 159989-64-7 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 503 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:838939 CAPLUS Full-text
DN 136:144717
TI Interferon and ribavirin combination therapy for chronic hepatitis C in human immunodeficiency virus-infected patients with congenital coagulation disorders
AU Sauleda, Silvia; Juarez, Alberto; Esteban, Juan I.; Altisent, Carmen; Ruiz, Isabel; Puig, Lluis; Esteban, Rafael; Guardia, Jaime
CS Centre de Transfusio i Banc de Teixits, Servei Catala de la Salut, Hospital Universitari Vall d'Hebron, Universitat Autonoma de Barcelona, Barcelona, 08035, Spain
SO Hepatology (Philadelphia, PA, United States) (2001), 34(5), 1035-1040
CODEN: HPTLD9; ISSN: 0270-9139
PB W. B. Saunders Co.
DT Journal
LA English
AB We have conducted an open, prospective trial to assess the safety and efficacy of interferon alfa-2b and ribavirin in combination for the treatment of chronic hepatitis C in human immunodeficiency virus (HIV)-infected hemophiliacs. Twenty hemophiliacs coinfected with HIV and hepatitis C virus (HCV), 18 of them under highly active antiretroviral therapy (HAART), with a mean CD4+ cell count of 490 ± 176 cells/mm3 and undetectable (n = 9) or low-level HIV RNA (<10,000 copies/mL; n = 11), were treated with interferon-alpha2b (3 MU thrice weekly) and ribavirin (800 mg/d) for 6 or 12 mo according to virol. response. Patients were monitored for tolerance and response at 4, 8, 12, 24, 36, and 48 wk during treatment and every other month thereafter. All 20 patients enrolled completed at least 6 mo of treatment with no major side effect requiring treatment withdrawal, dose reduction, or modification of HAART. Overall, 8 patients (40%) achieved a sustained virol. response at the end of the 6-mo post-treatment follow-up. Sustained responders had lower baseline HCV-RNA levels (5.7 ± 0.8 vs. 6.3 ± 0.4 log10 IU/mL, P = .041) but were otherwise similar to nonresponders. All sustained responders had a decrease in HCV-RNA level of at least 1 log per mo during the first 2 mo and undetectable levels at 6 mo. In conclusion, our results provide evidence that combination therapy with interferon and ribavirin is safe in HIV-infected

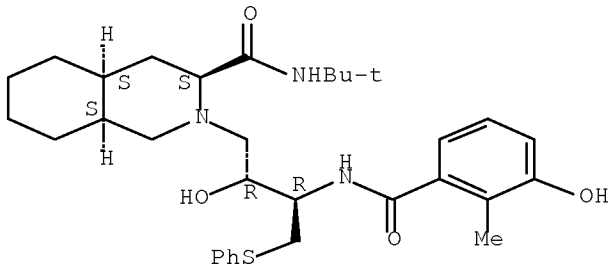
hemophiliacs with stable CD4 cell count and undetectable or low-level HIV replication, and leads to eradication of HCV in 40% of these patients.

IT 159989-64-7, Nelfinavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(interferon and ribavirin combination therapy for chronic hepatitis C in HIV infected humans with congenital coagulation disorders)

RN 159989-64-7 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 504 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:838390 CAPLUS Full-text

DN 137:52200

TI Nelfinavir suspension obtained from nelfinavir tablets has equivalent pharmacokinetic profile

AU Regazzi, M. B.; Seminari, E.; Villani, P.; Carriero, P. L.; Montagna, M.; Marubbi, F.; Maserati, R.

CS Department of Pharmacology, I.R.C.C.S. Policlinico San Matteo, University of Pavia, Pavia, Italy

SO Journal of Chemotherapy (Firenze, Italy) (2001), 13(5), 569-574
CODEN: JCHEEU; ISSN: 1120-009X

PB E.I.F.T. srl

DT Journal

LA English

AB The pharmacokinetics of nelfinavir tablets (A) and an oral simplified nelfinavir suspension (B) were studied. Twelve healthy volunteers randomly received either five 250-mg nelfinavir tablets or a simplified oral suspension obtained from tablets dissolved in water (nelfinavir 1250 mg in 100 mL of water) in a single dose before being crossed over to the second treatment after a one-week washout period. Blood samples were drawn up to 24 h after drug administration. Nelfinavir concns. in plasma were analyzed by a specific and validated reverse-phase high-performance liquid chromatog. assay (HPLC) with UV detection, and pharmacokinetic values were determined For the AUC0-∞ with means±SD of 31.71±7.85, 30.88±10.28 (μg/L) resp. for treatments B and A, the ratio (FB/A) was of 1.1 with a C.I. of 0.90-1.24. For Cmax with means±SD of 3.1±0.6 (treatment B) and 3.2±0.8 mg/mL (treatment A), the ratio was 1.0. with C.I. of 0.92- 1.08. The two treatments evidenced no significant differences in AUC0-∞ and Cmax values and the two-one sided t-test showed that the two prepns. are bioequivalent. There was no significant difference in Tmax between the liquid and tablets. Nelfinavir suspension might be a option

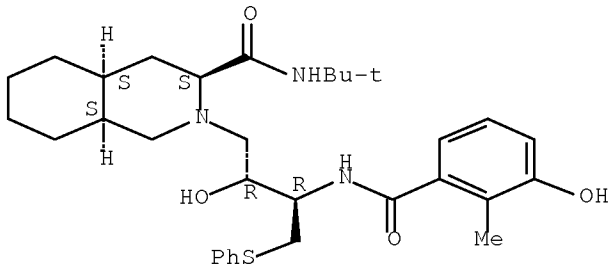
for treating HIV-infected patients with swallowing disturbances or compliance problems.

IT 159989-64-7, Nelfinavir
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nelfinavir suspension obtained from nelfinavir tablets has equivalent pharmacokinetic profile)

RN 159989-64-7 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 505 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:835754 CAPLUS Full-text

DN 136:133368

TI Pilot study of interferon-α with and without amantadine for the treatment of hepatitis C in HIV coinfected individuals on antiretroviral therapy

AU Sax, H.; Friedl, A.; Renner, E.; Steuerwald, M. H.; Weber, R.

CS Swiss HIV Cohort Study, Division of Infectious Diseases, University of Geneva Hospital, Geneva, CH-1211, Switz.

SO Infection (Munich, Germany) (2001), 29(5), 267-270
CODEN: IFTNAL; ISSN: 0300-8126

PB Urban & Vogel Medien und Medizin Verlagsgesellschaft mbH

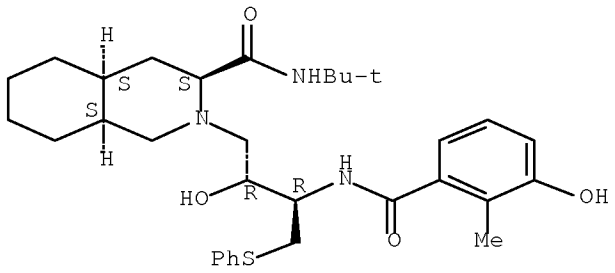
DT Journal

LA English

AB Concurrent potent therapy of hepatitis C (HCV) and HIV includes at least five antiviral drugs. Drug interactions, toxicity, tolerance and acceptance by patients of such treatment regimens are unknown. A prospective open randomized pilot trial was conducted to test interferon-α (6 million units/day for the 1st month followed by 6 million thrice weekly) and amantadine vs. interferon-α monotherapy for tolerability and feasibility among HIV and HCV co-infected patients on stable antiretroviral combination therapy. 1,013 HIV-infected patients were consecutively evaluated. 314 Were anti-HCV antibody pos.; only eight (2.4%) were eligible. Major reasons for exclusion were: normal transaminase levels (34%), ongoing i.v. drug use (33%), or recent change in antiretroviral therapy (31%). Study drugs were stopped in all of the seven patients enrolled because of side effects and/or failure of anti-HCV therapy. CD4 lymphocyte counts and HIV-1 RNA remained stable. Among patients on highly active antiretroviral therapy, the addition of interferon-α with or without amantadine was inefficient and poorly tolerated, but had no neg. influence on HIV infection. Eligibility for the study was unexpectedly low.

IT 159989-64-7, Nelfinavir
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(INF-α with/without amantadine for treatment of hepatitis C in HIV-infected humans on antiretroviral therapy)
RN 159989-64-7 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.

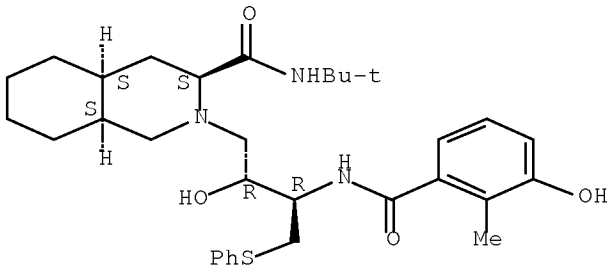


RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 506 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:834651 CAPLUS Full-text
DN 136:144710
TI A single-nucleotide polymorphism in the sterol-regulatory element-binding protein 1c gene is predictive of HIV-related hyperlipoproteinaemia
AU Miserez, Andre R.; Muller, Patrick Y.; Barella, Luca; Schwietert, Martin; Erb, Peter; Vernazza, Pietro L.; Battegay, Manuel
CS Swiss HIV Cohort Study, Cardiovascular Genetics, Department of Clinical-Biological Sciences, University of Basel, Basel, Switz.
SO AIDS (London, United Kingdom) (2001), 15(15), 2045-2049
CODEN: AIDSET; ISSN: 0269-9370
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB A single-nucleotide polymorphism (3'322C/G) was identified in the gene encoding a key cholesterol/triglyceride regulator, sterol-regulatory element-binding protein 1c (SREBP-1c). Although it did not alter the amino acid sequence, SREBP-1c-3'322C/G was predictive of highly active antiretroviral therapy-related hyperlipoproteinemia. Increases in cholesterol were less frequently associated with homozygous SREBP-1c-3'322G (genotype 22) than with heterozygous/homozygous SREBP-1c-3'322C (genotypes 11/12) and correlated with leptin and insulin increases, particularly in genotype 11/12 carriers. A functional mutation linked to SREBP-1c-3'322C/G or mRNA conformation differences may explain our findings.
IT 159989-64-7, Nelfinavir
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(single-nucleotide polymorphism in sterol-regulatory element-binding protein 1c gene is predictive of HIV-related hyperlipoproteinemia in humans)
RN 159989-64-7 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-

hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

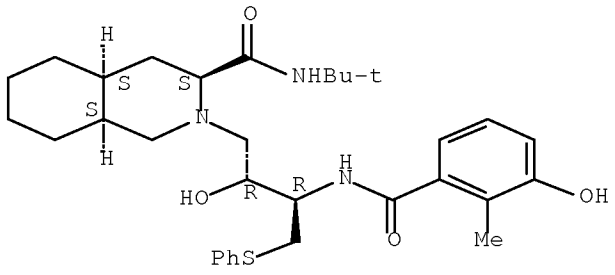
L11 ANSWER 507 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:834648 CAPLUS Full-text
DN 136:144709
TI Fat distribution and metabolic changes are strongly correlated and energy expenditure is increased in the HIV lipodystrophy syndrome
AU Kosmiski, Lisa A.; Kuritzkes, Daniel R.; Lichtenstein, Kenneth A.; Glueck, Deborah H.; Gourley, Patrick J.; Stamm, Elizabeth R.; Scherzinger, Ann L.; Eckel, Robert H.
CS Division of Endocrinology, Metabolism and Diabetes, Department of Medicine, University of Colorado Health Sciences Center, Denver, CO, USA
SO AIDS (London, United Kingdom) (2001), 15(15), 1993-2000
CODEN: AIDSET; ISSN: 0269-9370
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB To examine the relationships among protease inhibitor (PI) therapy, body fat distribution, and metabolic disturbances in the HIV lipodystrophy syndrome, a cross-sectional study was conducted in HIV primary care practices which included PI-treated patients with lipodystrophy (n = 14) and PI-treated (n = 13) and PI-naive (n = 5) patients without lipodystrophy. Body composition was assessed by phys. examination, dual-energy x-ray absorptiometry, and computed tomog. Insulin sensitivity (SI) was measured using the insulin-modified frequently sampled i.v. glucose tolerance test. Lipid profiles, other metabolic parameters, duration of HIV infection, CD4 lymphocyte counts, HIV-1 RNA load, and resting energy expenditure (REE) were also assessed. PI-treated patients with lipodystrophy were significantly less insulin-sensitive than PI-treated patients and PI-naive patients without any changes in fat distribution (SI(22) + 10-4 (min-1/μU/mL) vs. 3.2 + 10-4 and 4.6 + 10-4 (min-1/μU/mL), resp.; P < 0.001). Visceral adipose tissue area and other measures of central adiposity correlated strongly with metabolic disturbances as did the percent of total body fat present in the extremities; visceral adipose tissue was an independent predictor of insulin sensitivity and high-d. lipoprotein cholesterol levels. REE per kg lean body mass was significantly higher in the group with lipodystrophy compared to the groups without lipodystrophy (36.9 vs. 31.5 and 29.4 kcal/kg lean body mass; P < 0.001), and SI was strongly correlated with and was an independent predictor of REE in this population. Body fat distribution and metabolic disturbances are strongly correlated in the HIV lipodystrophy syndrome and REE is increased.
IT 159989-64-7, Nelfinavir

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fat distribution, metabolic changes, and increased energy expenditure in humans with HIV lipodystrophy syndrome)

RN 159989-64-7 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 508 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:834647 CAPLUS Full-text

DN 136:144708

TI Long-term quality of life outcomes in three antiretroviral treatment strategies for HIV-1 infection

AU Nieuwkerk, Pythia T.; Gisolf, Elisabeth H.; Reijers, Monique H. E.; Lange, Joep M. A.; Danner, Sven A.; Sprangers, Mirjam A. G.

CS NATIVE, PROMETHEUS and ADAM study groups, Department of Medical Psychology, Academic Medical Center, Amsterdam, Neth.

SO AIDS (London, United Kingdom) (2001), 15(15), 1985-1991
CODEN: AIDSET; ISSN: 0269-9370

PB Lippincott Williams & Wilkins

DT Journal

LA English

AB Objective: to compare changes in quality of life (QoL) over 96 wk in patients enrolled in a triple-therapy protocol, a treatment- intensification protocol, or an induction-maintenance therapy protocol, and to compare QoL between patients who continued and discontinued their antiretroviral regimen. Patients: naive patients enrolled in a triple-therapy protocol (zidovudine/lamivudine or stavudine/didanosine or stavudine/lamivudine supplemented with protease inhibitor therapy of choice) (n ≈ 35), a protocol of treatment intensification (ritonavir/saquinavir or ritonavir/saquinavir/stavudine) (n = 74) in which therapy was intensified with nucleoside analog(s) in cases of insufficient viral suppression, and a protocol of induction (saquinavir/nelfinavir/lamivudine/ stavudine) maintenance (saquinavir/nelfinavir or stavudine/nelfinavir) therapy (n = 50). Main outcome measure: changes from baseline in QoL assessed by the Medical Outcomes Study HIV Health Survey at weeks 0, 12, 24, 36, 48, 72 and 96. Results: patients in the triple-therapy and treatment-intensification protocols showed more favorable changes in phys. function, social function, mental health, energy/fatigue, health distress and overall QoL compared to patients in the induction-maintenance protocol, with patients in the first two protocols showing improvements in QoL and those in the induction-maintenance

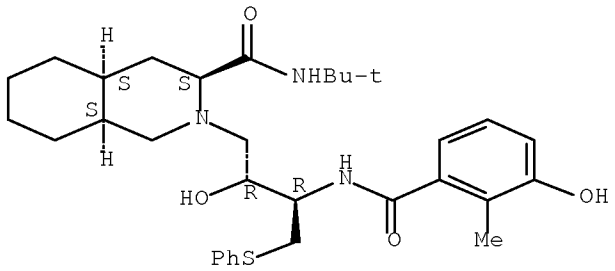
protocol showing declining or unchanged QoL. Patients who discontinued study medication due to insufficient efficacy, toxicities or at their own request showed less favorable changes in QoL compared with patients who continued their regimen. The highest proportion of discontinuations was within the induction-maintenance protocol. Conclusion: antiretroviral treatment strategies that are effective and tolerable have the potential to improve patients' QoL over 96 wk.

IT 159989-64-7, Nelfinavir
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(three antiretroviral treatment strategies for HIV-1 infection)

RN 159989-64-7 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 509 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:834646 CAPLUS Full-text

DN 137:57002

TI HIV-protease inhibitors alter retinoic acid synthesis

AU Toma, Emil; Devost, Dominic; Lan, Nathaly Chow; Bhat, Pangala V.

CS Department of Microbiology & Infectious Diseases, Centre hospitalier de l'Universite de Montreal, Montreal, QC, H2W 1T8, Can.

SO AIDS (London, United Kingdom) (2001), 15(15), 1979-1984
CODEN: AIDSET; ISSN: 0269-9370

PB Lippincott Williams & Wilkins

DT Journal

LA English

AB An increasing rate of highly-active antiretroviral therapy (HAART)-associated metabolic and morphol. abnormalities has been reported in HIV-infected persons. Some of them resemble retinoid-related adverse events, indicating alteration(s) of retinol metabolism or of retinoic acid-mediated signaling. Retinol levels in patients with or without HAART were evaluated and the effect of antiretroviral agents on retinal dehydrogenase (RALDH), a key enzyme involved in retinoic acid synthesis, was assessed. Plasma retinol levels, measured in six patients receiving HAART and in five others with no antiretroviral therapy, were correlated with levels of serum retinol-binding proteins. We then studied the effects of seven antiretroviral agents on RALDH activity and gene expression in a kidney-derived cell line (LLCPK). Plasma retinol levels in patients receiving HAART were decreased in comparison with those not receiving antiretroviral drugs (51 ± 5 vs. 66 ± 11 μg/dL; P = 0.03), whereas retinol-binding protein levels were increased (68 ± 18 vs. 45 ± 10

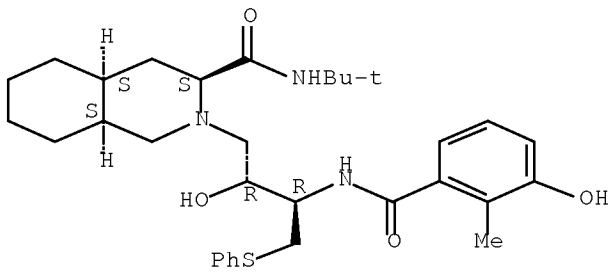
mg/L; P = 0.04). RALDH activity was heightened by ritonavir (24%), indinavir (17%), saquinavir (17%), zalcitabine (14%), delavirdine (12%) and nelfinavir (10%) and decreased (22%) by DMP-450. RALDH gene expression was induced only by indinavir. These data indicate that certain retinoid-like adverse effects in HAART-receiving patients are not due to higher retinol levels. Enhanced RALDH activity or/and gene expression by some protease inhibitors could increase retinoic acid concns. Elevated retinoic acid levels might be responsible for retinoid-like or other adverse effects due to alterations in the expression of retinoic acid-responsive genes.

IT 159989-64-7, Nelfinavir
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HIV-proteinase inhibitors alter retinoic acid synthesis)

RN 159989-64-7 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 510 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:834645 CAPLUS Full-text
DN 136:144707
TI Randomized, double-blind comparison of two nelfinavir doses plus nucleosides in HIV-infected patients (Agouron study 511)
AU Saag, Michael S.; Tebas, Pablo; Sension, Michael; Conant, Marcus; Myers, Robert; Chapman, Sharon K.; Anderson, Robert; Clendeninn, Neil
CS Viracept Collaborative Study Group, University of Alabama at Birmingham, Birmingham, AL, 35294-2050, USA
SO AIDS (London, United Kingdom) (2001), 15(15), 1971-1978
CODEN: AIDSET; ISSN: 0269-9370
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB Objective: to evaluate the safety and antiretroviral activity of nelfinavir mesylate at two doses as part of a combination regimen in HIV-infected, antiretroviral-naive patients. Design: phase III, multicenter, double-blind, placebo-controlled trial. Patients and methods: two-hundred and ninety-seven patients were randomized to one of three treatment groups: nelfinavir 750 mg three times daily (tid), nelfinavir 500 mg tid, or matching placebo, each in combination with open-label zidovudine (ZDV) 200 mg tid and lamivudine (3TC) 150 mg twice daily (bid). Data were analyzed on an intent-to-treat basis. Results: sixty-seven percent of patients receiving nelfinavir 750 mg tid, and 50% receiving nelfinavir 500 mg tid in combination with ZDV/3TC achieved HIV

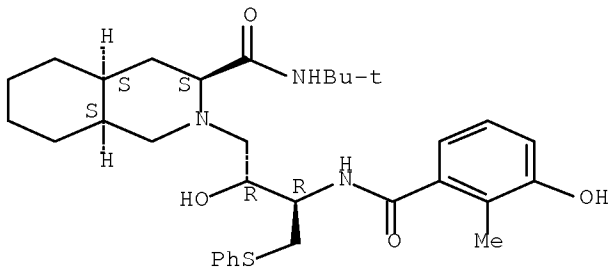
RNA < 400 copies/mL compared to 7% receiving ZDV/3TC plus placebo (P < 0.001); 55% and 30% of patients in the nelfinavir-containing arms achieved HIV RNA < 50 copies/mL at week 24. This compared with 4% in the placebo-containing arm. For patients continuing nelfinavir treatment (750 mg or 500 mg tid as treated) for a further 6 mo, the proportions achieving < 400 copies/mL at week 48 were 75% and 54% (P = 0.001) and < 50 copies/mL 61% and 37%, resp. (P = 0.004). The mean increases from baseline in CD4 cell counts were also durable in patients receiving the triple combination nelfinavir therapy. The range and incidence of adverse events was similar for the two nelfinavir-containing arms, with diarrhea being the most common adverse event. Conclusions: nelfinavir plus ZDV/3TC was superior to ZDV/3TC/placebo. In addition, the 750 mg tid nelfinavir dose was better than the 500 mg tid dose. Virol. responses were sustained over 12 mo.

IT 159989-64-7, Nelfinavir
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nelfinavir dosage plus nucleosides in HIV-infected humans)

RN 159989-64-7 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 511 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:834644 CAPLUS Full-text

DN 136:144706

TI Persistence of HIV-1 resistance in lymph node mononuclear cell RNA despite effective HAART

AU Lafeuillade, Alain; Khiri, Hacene; Chadapaud, Stephane; Hittinger, Gilles; Halfon, Philippe

CS Department of Infectious Diseases, General Hospital, Toulon, Fr.

SO AIDS (London, United Kingdom) (2001), 15(15), 1965-1969
CODEN: AIDSET; ISSN: 0269-9370

PB Lippincott Williams & Wilkins

DT Journal

LA English

AB Objective: To analyze the presence of genotypic and phenotypic resistance in lymph node mononuclear cells from patients with sustained undetectable plasma HIV-1 RNA with highly active antiretroviral therapy. Design: Cross-sectional study on 27 HIV-infected patients receiving triple therapy for a mean period of 232.8 ± 22.1 wk. Methods: HIV-1 RNA was measured in plasma and lymph node cells using PCR. Reverse transcriptase and protease genes were sequenced from HIV-1 RNA obtained from lymph node cells and from peripheral blood mononuclear

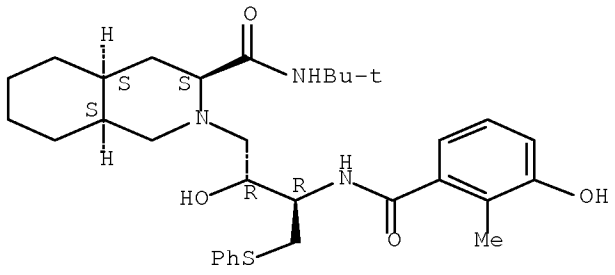
cell proviral DNA using a com. available kit (TruGene). Phenotypic resistance was assessed by using a recombinant virus assay (AntiVirogram). Results: Mutations were not found in lymph node mononuclear cell RNA in six out of nine patients on first-line regimens although they were detected in 15 out of 18 who received prior suboptimal combinations. Phenotypic resistance was confirmed in most of these cases. These patterns of resistance were closely related to patients' history of antiretroviral therapy and genotypic anal. of plasma HIV-1 RNA taken just before initiation of the current regimen. In half the patients analyzed, resistance mutations found in lymph nodes were not always detected in archival proviral DNA from blood cells. Mean levels of HIV-1 RNA in lymph node cells were not different in patients exhibiting resistance compared with those harboring wild-type viruses. Conclusion: These data demonstrate that resistant HIV-1 is produced in lymphoid tissues for prolonged periods despite effective therapy. The mechanism could represent a release from previously infected cells rather than new cycles of cellular infection.

IT 159989-64-7, Nelfinavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HIV-1 resistance in lymph node mononuclear cell RNA despite effective HAART in humans)

RN 159989-64-7 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 512 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:833855 CAPLUS Full-text
DN 135:352760
TI Inhibition of taxane metabolism
IN Synold, Timothy W.; Doroshow, James H.
PA USA
SO U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 20010041706	A1	20011115	US 2001-814072	20010322 <--
PRAI US 2000-191828P	P	20000324		

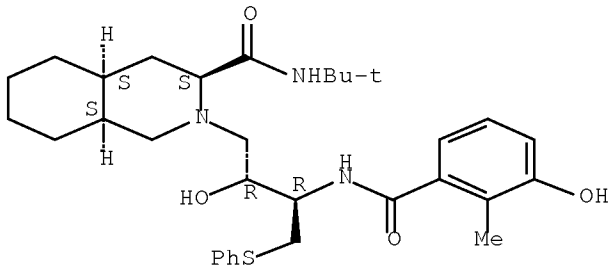
AB Methods are disclosed for the inhibition of taxane metabolism in patients receiving anticancer taxane treatment, in which an effective amount of a CYP3A4 inhibitor and a CYP2C8 inhibitor are administered to the patient.

IT 159989-64-7, Nelfinavir
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of taxane metabolism)

RN 159989-64-7 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 513 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:831902 CAPLUS Full-text

DN 136:247758

TI Synthesis and anti-HIV activity of glucose-containing prodrugs derived from saquinavir, indinavir and nelfinavir

AU Rouquayrol, Marielle; Gaucher, Berangere; Greiner, Jacques; Aubertin, Anne-Marie; Vierling, Pierre; Guedj, Roger

CS Parc Valrose, Laboratoire de Chimie Bio-Organique, Universite de Nice Sophia-Antipolis, UMR 6001 CNRS, Nice, F-06108, Fr.

SO Carbohydrate Research (2001), 336(3), 161-180
CODEN: CRBRAT; ISSN: 0008-6215

PB Elsevier Science Ltd.

DT Journal

LA English

OS CASREACT 136:247758

AB With the aim at improving the transport of the current HIV protease inhibitors across the intestinal and blood brain barriers and their penetration into the central nervous system, the synthesis of various acyl and carbamoyl glucose-containing prodrugs derived from saquinavir, indinavir and nelfinavir, their in vitro stability with respect to hydrolysis, and their anti-HIV activity have been investigated. D-Glucose, which is actively transported across these barriers, was connected through its 3-hydroxyl to these anti-proteases via a linker. The liberation of the active free drug during the incubation time of the prodrugs with the cells was found to be crucial for HIV inhibition. The labile ester linking of the glucose-containing moiety to the peptidomimetic hydroxyl of saquinavir or to the indinavir C-8 hydroxyl, which is not part of the transition state isostere, is not an obstacle for anti-HIV activity. This is not the case for its stable carbamate linking to the peptidomimetic hydroxyl of saquinavir, indinavir and nelfinavir. The chemical stability with respect to hydrolysis of some of the saquinavir and indinavir prodrugs reported here, the liberation rate of the active free drug and the HIV

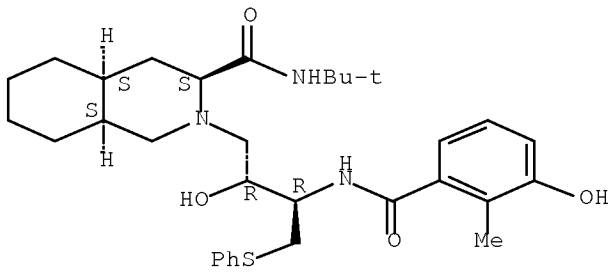
inhibitory potency are acceptable for an in vivo use of these prodrugs. These glucose-linked ester and carbamate prodrugs display a promising therapeutic potential provided that their bioavailability, penetration into the HIV sanctuaries, and/or the liberation of the active free drug from the carbamate prodrugs are improved. Furthermore, no cytotoxicity was detected for the prodrugs for concns. as high as 10 or even 100 μM, thus indicating an encouraging therapeutic index.

IT 159989-64-7, Nelfinavir
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(synthesis and anti-HIV activity of glucose-containing prodrugs derived from saquinavir, indinavir, and nelfinavir)

RN 159989-64-7 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 514 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:824699 CAPLUS Full-text

DN 136:128646

TI Impact of HIV type 1 drug resistance mutations and phenotypic resistance profile on virologic response to salvage therapy

AU Ross, Lisa; Liao, Qiming; Gao, Haitao; Pham, Sissi; Tolson, Jerry; Hertogs, Kurt; Larder, Brendan; Saag, Michael S.

CS GlaxoSmithKline, Research Triangle Park, NC, 27709, USA

SO AIDS Research and Human Retroviruses (2001), 17(15), 1379-1385
CODEN: ARHRE7; ISSN: 0889-2229

PB Mary Ann Liebert, Inc.

DT Journal

LA English

AB This study examines the association between presence of drug resistance mutations and phenotypic resistance at baseline to virol. response to salvage therapy in a community setting. The study population consisted of 58 antiretroviral drug-experienced patients with HIV-1 infection who had recently switched therapy because of virol. failure. Drug resistance mutations in the reverse transcriptase- and protease-coding regions and phenotypic susceptibility to 13 antiretroviral drugs were assessed at baseline. Plasma HIV-1 RNA levels were assessed at baseline and at subsequent clinic visits. Results showed that three variables were significant in predicting virol. response: HIV-1 levels at baseline, number of protease mutations, and phenotypic sensitivity score for the regimen at baseline. For four drugs there was a significant association between the presence of specific drug

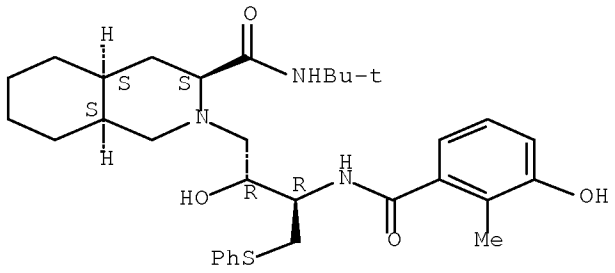
resistance mutations and >10-fold phenotypic resistance to that drug. With phenotypic resistance defined as >4-fold resistance, the association between specific drug resistance mutations and phenotypic resistance was significant for seven drugs. Overall, these data show that phenotypic susceptibility and absence of drug resistance mutations, particularly protease mutations, are significant predictors of virol. response. For several drugs, specific combinations of drug resistance mutations are associated with decreased phenotypic susceptibility and might provide useful clin. guidelines in selecting therapeutic options.

IT 159989-64-7, Nelfinavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HIV type 1 drug resistance mutations and phenotypic resistance profile on virol. response to salvage therapy)

RN 159989-64-7 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



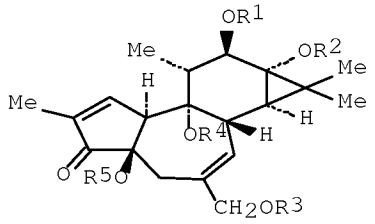
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 515 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:816455 CAPLUS Full-text
DN 135:348871
TI Antiviral compositions containing phorbol derivatives as the main active ingredient
IN Hattori, Masao; Yamamoto, Naoki; Mori, Masao
PA Lead Chemical Co., Ltd, Japan
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001082927	A1	20011108	WO 2000-JP2913	20000502 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,

CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI WO 2000-JP2913 20000502
OS MARPAT 135:348871
GI



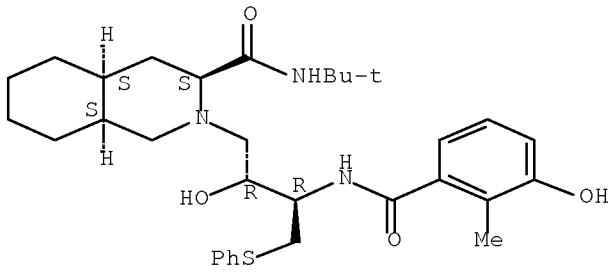
I

AB Described are antiviral compns. containing as the active ingredients: (i) phorbol derivs. which are represented by the general formula (I; wherein R1, R2, R3, R4 and R5 independently represent each hydrogen, an aliphatic carboxylate or an aromatic carboxylate.), have a ratio r = CC0/IC100 of 2 or more (wherein IC100 represents the concentration at which the cell pathogenic effect (CPE) of HIV-1 in MT-4 cells is inhibited at a ratio of 100; and CC0 represents the concentration at which the survival of MT-4 cells is reduced in a cell proliferation test), and show activation of protein kinase C (PKC) at a concentration of 10 ng/mL by 30% or less; and (ii) a chemical capable of suppressing or inhibiting the replication process or the maturation process of viruses. These compns. are efficacious particularly against human immunodeficiency virus (HIV). Thus, Croton tiglium seeds (3 kg) was refluxed with MeOH (10 L + 3) and the combined methanol solution was concentrated under reduced pressure to give an oil (763 g) which was suspended in 90% aqueous MeOH (7 L) and extracted with hexane (4 L + 3) and then with ether (4 L + 3). The combined ether extract was concentrated to give a resin-like substance (150 g) which was subjected to silica gel chromatog. and medium pressure liquid chromatog. to give 13-O-tigloylphorbol-20-(9Z,12Z- octadecadienoate) 60, 13-O-acetylphorbol-20-(9Z,12Z-octadecadienoate) 153, 12-O-dodecanoylphorbol-13-(2-methylbutyrate) 21, 12-O-(2- methylbutyroyl)phorbol-13-dodecanoate 30, 12-O-acetylphorbol-13-tiglate 35, 12-O-acetylphobol-13-decanoate 74, 12-O-decanoylphorbol-13-(2- methylbutyrate) 57, 12-O-tigloylphorbol-13-(2-methylbutyrate) 12, and 12-O-tetradecanoylphorbol-13-acetate 110 mg. Derivatization of these compds. by saponification, selective hydrolysis, esterification with acetic anhydride, benzoyl chloride, or butyryl chloride, reduction, or methylation, etc. gave phorbol, isophorbol, 4-deoxy-4α-phorbol, 13-O-acetylphorbol, phorbol-12,13-diacetate, 13-O-acetylcrotophorbolone- enol-20-linoleate, 12-O-tetradecanoylphorbol-13,20-diacetate, 4α-phorbol-12,13,20-triacetate, 4α-phorbol-4,12,13,20-tetraacetate, phorbol-12,13,20-triacetate, lumiphorbol-12,13,20- triacetate, 3-deoxo-3β-hydroxyphorbol-12,13,20-triacetate, 4-O-methylphorbol-12,13,20-triacetate, phorbol-4,9,12,13,20-pentaacetate, phorbol-12,13,20-tribenzoate, and 4α-phorbol-12,13,20-tributyrate. In assays for testing anti-HIV activity and PKC activation activity, 12-O-acetylphobol-13-decanoate showed IC100 and CC0 (defined as above) of 0.0076 and 62.5, resp., with r ratio of 8,220 and exhibited 0 and 17% PKC activation at 10 ng/mL and 17 μg/mL, resp.

IT 159989-64-7, Nelfinavir
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor of protease-mediated synthesis of HIV core protein, antiviral composition containing; antiviral compns. against HIV-1 containing phorbol

derivs. of Croton tiglium and their derivs. as active ingredients)
RN 159989-64-7 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 516 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:816447 CAPLUS Full-text
DN 135:352830
TI Methods of, and HIV protease inhibitor compounds for, inhibiting calpains, and therapeutic use thereof
IN De Petrillo, Paolo B.; Wan, Wenshuai
PA United States Dept. of Health and Human Services, USA
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001082919	A2	20011108	WO 2001-US40652	20010502 <--
	WO 2001082919	A3	20020510		
	WO 2001082919	B1	20020725		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001059817	A5	20011112	AU 2001-59817	20010502 <--
	US 20020115665	A1	20020822	US 2001-847872	20010502 <--
	US 6448245	B2	20020910		
PRAI	US 2000-202378P	P	20000504		
	WO 2001-US40652	W	20010502		

OS MARPAT 135:352830
AB A method is disclosed for inhibiting calpain by contacting calpain with one or more HIV protease inhibitors or analogs. Included are embodiments for identifying subjects at risk of suffering calpain-mediated physiol. damage and administering to them the HIV protease inhibitors or analogs. Alternatively, a

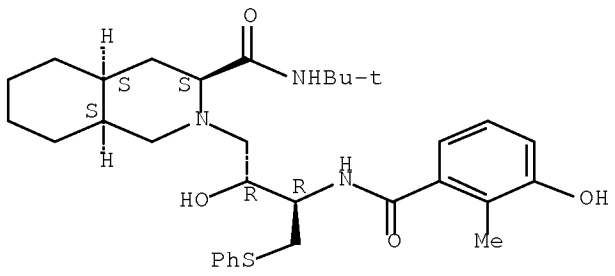
compound may be administered to a subject following an actual event implicating activation of calpain. Also included are methods of treating or preventing calpain-mediated physiol. damage in a subject by administering to the subject a therapeutically effective amount of a pharmaceutical composition which includes at least one HIV protease inhibitor or analog. The pharmaceutical compns. can be used in the treatment of a variety of conditions or diseases implicated by or associated with calpain activation, including cardiovascular diseases.

IT 159989-64-7, Nelfinavir
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HIV protease inhibitors for calpain inhibition, and therapeutic use)

RN 159989-64-7 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 517 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:812202 CAPLUS Full-text

DN 136:95645

TI Impaired response to HAART in HIV-infected individuals with high autonomic nervous system activity

AU Cole, Steve W.; Naliboff, Bruce D.; Kemeny, Margaret E.; Griswold, Marshall P.; Fahey, John L.; Zack, Jerome A.

CS Department of Medicine, University of California, Los Angeles, CA, 90095, USA

SO Proceedings of the National Academy of Sciences of the United States of America (2001), 98(22), 12695-12700
CODEN: PNASA6; ISSN: 0027-8424

PB National Academy of Sciences

DT Journal

LA English

AB Neurotransmitters can accelerate HIV-1 replication in vitro, leading us to examine whether differences in autonomic nervous system (ANS) activity might promote residual HIV-1 replication in patients treated with highly active antiretroviral therapy. Patients who showed constitutively high levels of ANS activity before highly active antiretroviral therapy experienced poorer suppression of plasma viral load and poorer CD4+ T cell recovery over 3-11 mo of therapy. ANS activity was not related to demog. or behavioral characteristics that might influence pathogenesis. However, the ANS neurotransmitter norepinephrine enhanced replication of both CCR5- and CXCR4-tropic strains of HIV-1 in vitro via chemokine receptor up-regulation and

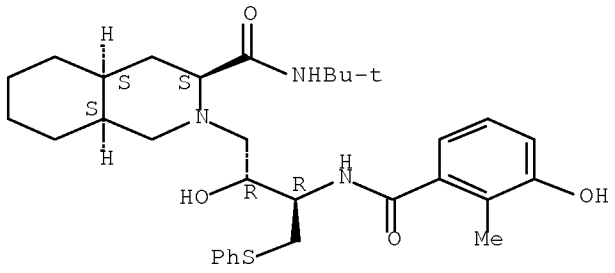
enhanced viral gene expression, suggesting that neural activity may directly promote residual viral replication.

IT 159989-64-7, Nelfinavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(impaired response to HAART in HIV-infected humans with high autonomic nervous system activity)

RN 159989-64-7 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 518 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:811051 CAPLUS Full-text

DN 136:95644

TI Virologic and immunologic parameters that predict clinical response of AIDS-associated Kaposi's sarcoma to highly active antiretroviral therapy

AU Pellet, C.; Chevret, S.; Blum, L.; Gauville, C.; Hurault, M.; Blanchard, G.; Agbalika, F.; Lascoux, C.; Ponscarme, D.; Morel, P.; Calvo, F.; Lebbe, C.

CS Laboratory of Pharmacology, Hopital Saint-Louis, Paris, 75010, Fr.

SO Journal of Investigative Dermatology (2001), 117(4), 858-863
CODEN: JIDEAE; ISSN: 0022-202X

PB Blackwell Science, Inc.

DT Journal

LA English

AB The purpose of the work was to assess the predictive value of biol. factors on the efficacy of highly active antiretroviral therapy alone or combined with chemotherapy on AIDS-associated Kaposi's sarcoma. Twenty-six AIDS-Kaposi's sarcoma patients who started therapy with protease inhibitors were investigated. No baseline chemotherapy was associated with less severe initial clin. status. Median follow-up was 652 d. The main outcome measures were as follows: best Kaposi's sarcoma clin. response; Kaposi's-sarcoma-associated herpesviral load in peripheral blood mononuclear cells using real-time quant. polymerase chain reaction (non-detectable of less than 100 copies per μg); human immunodeficiency viral charge in plasma (non-detectable if less than 200 copies per mL); and CD4 lymphocyte count. Time to undetectable Kaposi's-sarcoma-associated herpesviral load, time to undetectable human immunodeficiency viral charge, and time to CD4 ≥ 150 per μl were also recorded over time, from 2 mo measurements. Patients were staged according to the AIDS Clin. Trials Group-based tumor, immune, systemic staging system criteria. At baseline, Kaposi's sarcoma was progressive for 25 (96%) of the 26 enrolled

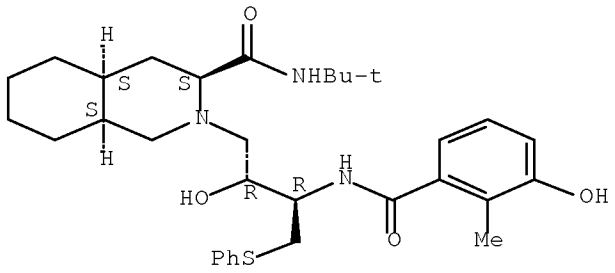
patients. Complete or partial response to highly active antiretroviral therapy alone or combined with chemotherapy was achieved in 22 patients (85%). Median time to clin. response was estimated at 251 d. Clin. response was faster in patients without chemotherapy at baseline (p = 0.003) as well as in patients not previously treated with reverse transcriptase inhibitors (p = 0.0012). Using univariable analyses, predictive factors of clin. response were undetectable Kaposi's-sarcoma-associated herpesviremia (p = 0.013), undetectable human immunodeficiency viremia (p = 0.03), and relative variation of CD4 lymphocytes (p = 0.004). Using multivariable anal., undetectable Kaposi's-sarcoma-associated herpesviremia (p = 0.009) and relative variation of CD4 (p = 0.005) were independently selected as having a predictive value for clin. response. Occurrence of nondetection of either Kaposi's-sarcoma-associated herpesvirus or human immunodeficiency virus was not associated with baseline CD4 value. Kaposi's-sarcoma-associated herpesvirus quant. viral charge is an independent predictive factor of the efficacy of highly active antiretroviral therapy on AIDS-Kaposi's sarcoma. Our results support immune reconstitution as a mechanism of response of Kaposi's sarcoma to highly active antiretroviral therapy.

IT 159989-64-7, Nelfinavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(predictive value of biol. factors on efficacy of highly active antiretroviral therapy alone or combined with chemotherapy on AIDS-associated Kaposi's sarcoma.)

RN 159989-64-7 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 519 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:811022 CAPLUS Full-text
DN 136:112259
TI Effect of highly active antiretroviral therapy on fat, lean, and bone mass in HIV-seropositive men and women
AU McDermott, Ann Yelmokas; Shevitz, Abby; Knox, Tamsin; Roubenoff, Ronenn; Kehayias, Joseph; Gorbach, Sherwood
CS Department of Family Medicine and Community Health, Boston, MA, USA
SO American Journal of Clinical Nutrition (2001), 74(5), 679-686
CODEN: AJCNAC; ISSN: 0002-9165
PB American Society for Clinical Nutrition
DT Journal
LA English

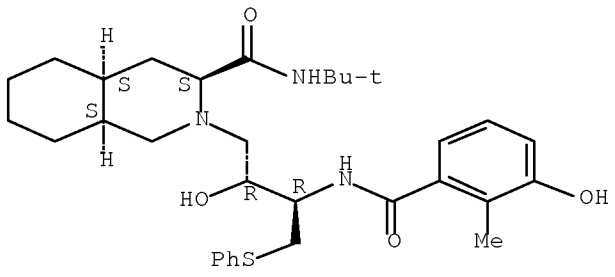
AB Alterations in body composition have been reported in HIV-pos. adults receiving highly active antiretroviral therapy (HAART), but the magnitude and potential determinants of these changes are unclear. We compared total and regional body composition, as measured by dual-energy x-ray absorptiometry, in 203 HIV-pos. men and 62 HIV-pos. women according to HAART. This was a cross-sectional anal. of a cohort study of nutrition and HIV infection. After adjustment for age, weight, race, and exercise habits, total weight and fat mass did not differ significantly in men or women by HAART. Trunk fat was greater in men (1.0 kg; P < 0.001) and women (1.4 kg; P = 0.005) and leg fat was lower in men (-1.0 kg; P < 0.001) and women (-1.5 kg, P = 0.005) receiving HAART than in those not. This corresponded to a greater percentage of total fat mass located in the trunk (men: 7.5%, P < 0.001; women: 5.1%, P = 0.02). Lean mass was also greater with longer duration of HAART in men (P < 0.002). In men receiving HAART, total and regional bone mineral content were less than in the men not receiving HAART (P < 0.001). These effects increased with longer duration of HAART. Protease inhibitors were associated with the largest differences in regional fat. HAART is associated with redistribution of fat mass from the legs to the trunk, despite no significant differences in total fat mass or weight In men, HAART is also associated with a reduction in bone mineral content, suggesting that HAART increases the risk of central obesity and osteoporosis.

IT 159989-64-7, Nelfinavir
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(highly active antiretroviral therapy effect on fat, lean, and bone mass in HIV-seropos. men and women)

RN 159989-64-7 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.

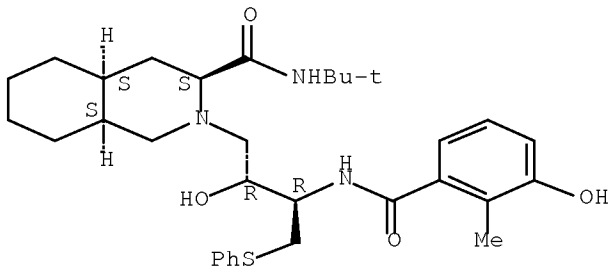


RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 520 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:810625 CAPLUS Full-text
DN 137:56997
TI Hepatotoxicity with antiretroviral treatment of pregnant women
AU Hill, James B.; Sheffield, Jeanne S.; Zeeman, Gerda G.; Wendel, George D.
CS Department of Obstetrics and Gynecology, University of Texas Southwestern Medical Center, Dallas, TX, USA
SO Obstetrics & Gynecology (New York, NY, United States) (2001), 98(5, Pt. 2), 909-911
CODEN: OBGNAS; ISSN: 0029-7844
PB Elsevier Science Inc.

DT Journal
LA English
AB BACKGROUND:Hepatotoxicity in adults with human immunodeficiency virus (HIV) infection has been associated with all classes of antiretroviral drugs and coinfection with hepatitis B and C virus. We treated two HIV-infected pregnant women in whom hepatotoxicity developed after initiating antiretroviral therapy. CASES:The first woman developed icterus, jaundice, hyperbilirubinemia, and elevated serum aminotransferase levels approx. 5 mo after beginning combination antiretroviral therapy with zidovudine, lamivudine, and efavirenz. Serum aminotransferase abnormalities improved after discontinuation of antiretroviral medications. The second woman had similar symptoms and laboratory abnormalities 3 mo after initiation of zidovudine, lamivudine, and nelfinavir. Despite initial improvement after discontinuing her antiretroviral medications, fulminant hepatic failure developed and she died. Both patients tested neg. for hepatitis A, B, and C; Epstein-Barr virus; and cytomegalovirus. There was no history of illicit drug use, alc. use, or blood transfusions in either case. CONCLUSION:We emphasize the need for careful monitoring for hepatotoxicity after initiation of antiretroviral therapy.
IT 159989-64-7, Nelfinavir
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiviral drugs hepatotoxicity in HIV-infected pregnant women)
RN 159989-64-7 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 521 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:801259 CAPLUS Full-text
DN 136:95639
TI Antiretroviral prophylaxis for community exposure to the human immunodeficiency virus in Switzerland, 1997-2000
AU Bernasconi, Enos; Jost, Joseph; Ledergerber, Bruno; Hirschel, Bernard; Francioli, Patrick; Sudre, Philippe
CS Infectious Diseases Unit, Department of Medicine, Regional Hospital, Lugano, Switz.
SO Swiss Medical Weekly (2001), 131(29/30), 433-437
CODEN: SMWWAI; ISSN: 1424-7860
PB EMH Swiss Medical Publishers Ltd.
DT Journal
LA English

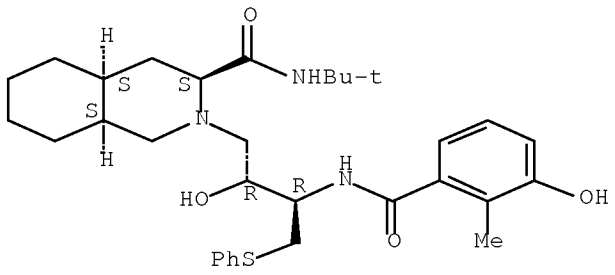
AB To analyze the data from Swiss nationwide voluntary reporting on non-occupational HIV-postexposure prophylaxis (HIV-PEP) by prescribing physicians. One hundred and seventy-six persons, who received antiretroviral prophylaxis for community exposure to HIV between Dec. 1997 and Mar. 2000, were included in this prospective cohort study with standardized data collection. Information on the source, the exposed person, type of exposure, treatment, and outcome was reported by physicians on a voluntary basis to three co-ordinating centers. HIV-PEP was prescribed predominantly following sexual exposure (69%). Needle injury was the second most common type of exposure (19% of all exposures), mostly occurring in a non-health care related "professional" setting (ie, housekeepers, concierges [caretakers], and policemen). Needle sharing accounted for only 4% of all cases of exposure. The HIV status of the source often remained unknown (56%). Most patients received a combination of three antiretroviral drugs (zidovudine/lamivudine/nelfinavir in 34.1%; zidovudine/lamivudine/indinavir in 22.8%; zidovudine/lamivudine/nevirapine in 18.6%; various triple combinations in 13.8%). Follow-up information was available for 86 patients. In this group 78 (91%) completed at least one week of prophylaxis. Side-effects were common (70.9%), particularly diarrhea (29.6%) and nausea (20.9%). Two patients experienced severe side effects, nephrolithiasis with sepsis, and toxic hepatitis, resp. In most of the cases where HIV-PEP was prescribed the indication was questionable, with the HIV status of the source unknown. The role of HIV-PEP as part of HIV prevention programs should be well defined in view of the cost and potential for causing severe side-effects.

IT 159989-64-7, Nelfinavir
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiretroviral prophylaxis for community exposure to the human immunodeficiency virus in Switzerland)

RN 159989-64-7 CAPLUS

CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 522 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:799024 CAPLUS Full-text

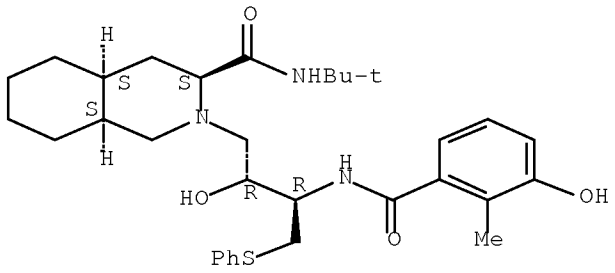
DN 136:95633

TI DPC 681 and DPC 684: potent, selective inhibitors of human immunodeficiency virus protease active against clinically relevant mutant variants

AU Kaltenbach, Robert F., III; Trainor, George; Getman, Daniel; Harris, Greg; Garber, Sena; Cordova, Beverly; Bacheler, Lee; Jeffrey, Susan; Logue,

Kelly; Cawood, Pamela; Klabe, Ronald; Diamond, Sharon; Davies, Marc; Saye, Joanne; Jona, Janan; Erickson-Viitanen, Susan
CS Departments of Chemistry and Physical Sciences, Virology, Drug Metabolism, Pharmacy and Safety Assessment, DuPont Pharmaceuticals Co., Wilmington, DE, 19880, USA
SO Antimicrobial Agents and Chemotherapy (2001), 45(11), 3021-3028
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB Human immunodeficiency virus (HIV) protease inhibitors (PIs) are important components of many highly active antiretroviral therapy regimens. However, development of phenotypic and/or genotypic resistance can occur, including cross-resistance to other PIs. Development of resistance takes place because trough levels of free drug are inadequate to suppress preexisting resistant mutant variants and/or to inhibit de novo-generated resistant mutant variants. There is thus a need for new PIs, which are more potent against mutant variants of HIV and show higher levels of free drug at the trough. We have optimized a series of substituted sulfonamides and evaluated the inhibitors against laboratory strains and clin. isolates of HIV type 1 (HIV-1), including viruses with mutations in the protease gene. In addition, serum protein binding was determined to estimate total drug requirements for 90% suppression of virus replication (plasma IC90). Two compds. resulting from our studies, designated DPC 681 and DPC 684, are potent and selective inhibitors of HIV protease with IC90s for wild-type HIV-1 of 4 to 40 nM. DPC 681 and DPC 684 showed no loss in potency toward recombinant mutant HIVs with the D30N mutation and a fivefold or smaller loss in potency toward mutant variants with three to five amino acid substitutions. A panel of chimeric viruses constructed from clin. samples from patients who failed PI-containing regimens and containing 5 to 11 mutations, including positions 10, 32, 46, 47, 50, 54, 63, 71, 82, 84, and 90 had mean IC50 values of <20 nM for DPC 681 and DPC 681, resp. In contrast, marketed PIs had mean IC50 values ranging from 200 nM (amprenavir) to >900 nM (nelfinavir).
IT 159989-64-7, (Nelfinavir).
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(activity of HIV-protease inhibitors DPC 681 and DPC 684 against clin. relevant mutant variants)
RN 159989-64-7 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

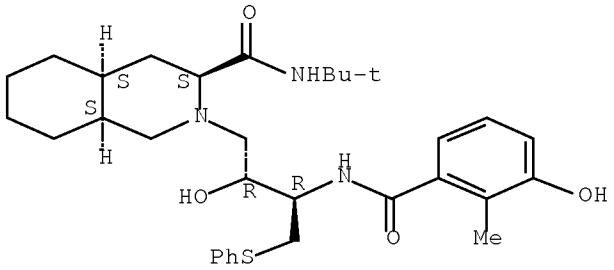
Absolute stereochemistry.



RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 523 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:790092 CAPLUS Full-text
DN 136:144693
TI Early detection of mixed mutations selected by antiretroviral agents in HIV-infected primary human lymphocytes
AU Schinazi, Raymond F.; Schlueter-Wirtz, Susan; Stuyver, Lieven
CS Department of Veterans Affairs, Decatur, GA, USA
SO Antiviral Chemistry & Chemotherapy (2001), 12(Suppl. 1), 61-65
CODEN: ACCHEH; ISSN: 0956-3202
PB International Medical Press
DT Journal
LA English
AB A growing concern in the pursuit of new therapies for HIV-1 infection is the potential for the virus to develop drug resistance. With the advent of modern antiretroviral therapy and the common use of combined modalities, it is difficult to identify in the clinic the mutations associated with a specific drug. In general, drug selection of mutants using a relevant cell system, such as primary human lymphocytes, is a good prognosticator of what will happen in humans. In this study, HIV-infected human peripheral blood mononuclear cells were exposed, at a concentration of 1- to 10-fold the median effective antiviral concentration, to the nucleosides (-)-β-2',3'-dideoxy-3'-thia-5-fluorocytidine [(-)-FTC], (-)-β-2',3'-dideoxy-3'-thiacytidine (3TC), 3'-azido-2',3'- dideoxyuridine (CS-87, AZDU), 3'-azido-2',3'-dideoxy-5-methylcytidine (CS-92, AZMC), 2',3'-didehydro-3'-deoxythymidine (d4T), β-L-2',3'-didehydro-2',3'-dideoxy-5-fluorocytidine (β-L-D4FC), β-L-2',3'-dideoxyadenine SATE [β-L-ddAMP-bis(tbuty(SATE))], β-L-5-fluoro-2',3'-dideoxycytidine (L-FddC), and the protease inhibitors nelfinavir and amprenavir (VX-478). Virus from the culture supernatant was amplified by PCR and analyzed by both HIV-1 reverse transcriptase and protease line probe assay. All the L-nucleoside analogs tested selected for the V184 mutation, including the L-pyrimidine nucleosides 3TC (-)-FTC, β-L-FddC, β-L-D4FC and the β-L-purine nucleoside. β-L-D4FC also selected for K/R65 in addition to V184, indicating that these two mutations are linked and compatible in vitro. No pattern of mutations leading to resistance or reduced susceptibility was discerned with d4T. Rapid genotyping anal. revealed the different kinetics and mutations obtained by in vitro selection in HIV-infected cells exposed to nucleoside analogs and protease inhibitors.
IT 159989-64-7, Nelfinavir
RL: PAC (Pharmacological activity); BIOL (Biological study)
(early detection of mixed mutations selected by antiretroviral agents in HIV-infected primary human lymphocytes)
RN 159989-64-7 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.

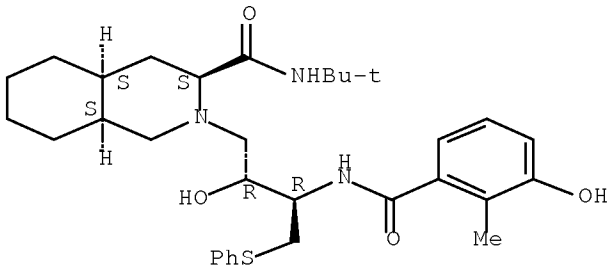


RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 524 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:789951 CAPLUS Full-text
DN 136:112137
TI Rational use of in vitro P-glycoprotein assays in drug discovery
AU Polli, Joseph W.; Wring, Stephen A.; Humphreys, Joan E.; Huang, Liyue; Morgan, Jonathon B.; Webster, Lindsey O.; Serabjit-Singh, Cosette S.
CS Preclinical Drug Metabolism and Pharmacokinetics, GlaxoSmithKline, Inc., Research Triangle Park, NC, USA
SO Journal of Pharmacology and Experimental Therapeutics (2001), 299(2), 620-628
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB P-glycoprotein (Pgp) affects the absorption, distribution, and clearance of a variety of compds. Thus, identification of compds. that are Pgp substrates can aid drug candidate selection and optimization. Our goal was to evaluate three assays used to determine whether compds. are Pgp substrates. Sixty-six compds. were tested in monolayer efflux, ATPase, and calcein-AM assays. Assay results yielded two categories of compds. Category I (n = 35) exhibited concordance across the assays. Category II (n = 31) revealed differences among the assays that related to the apparent permeability (Papp) of the compds. Within category II, two groups were discerned based on the absence (group IIA, n = 10, nontransported substrates) or presence (group IIB, n = 21, transported substrates) of monolayer efflux. Detection of efflux (group IIB) was associated with compds. having low/moderate Papp values (mean = 16.6 nm/s), whereas inability to detect efflux (group IIA) was associated with compds. having high Papp values (mean = 535 nm/s). The calcein-AM and ATPase assays revealed Pgp interactions for highly permeable group IIA compds. but were less responsive than monolayer efflux for low/moderate Papp compds. of group IIB. All assays detected substrates across a broad range of Papp, but the efflux assay was more prone to fail at high Papp, whereas the calcein-AM and ATPase assays were more prone to fail at low Papp. When Papp is low, efflux is a greater factor in the disposition of Pgp substrates. The efflux assay is more reliable at low/moderate Papp and is the method of choice for evaluating drug candidates despite low throughput and reliance on liquid chromatog. with tandem mass spectrometry.
IT 159989-64-7, Nelfinavir
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); BIOL (Biological study)
(comparison of in vitro P-glycoprotein assays used in drug discovery to determine drugs that are Pgp substrates)
RN 159989-64-7 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-

hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.

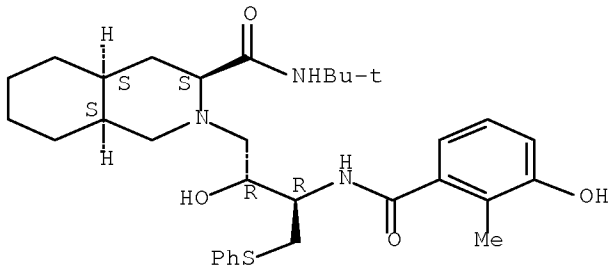


RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 525 OF 1028 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2001:785088 CAPLUS Full-text
DN 136:95626
TI Emergence of drug resistance mutations in a group of HIV-infected children taking nelfinavir-containing regimens
AU Fitzgibbon, Joseph E.; Gaur, Sunanda; Walsman, Scott M.; Janahi, Mohammed; Whitley-Williams, Patricia; John, Joseph F., Jr.
CS Division of Allergy, Immunology, and Infectious Diseases, Department of Medicine, University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School, New Brunswick, NJ, 08903, USA
SO AIDS Research and Human Retroviruses (2001), 17(14), 1321-1328
CODEN: ARHRE7; ISSN: 0889-2229
PB Mary Ann Liebert, Inc.
DT Journal
LA English
AB HIV-1-infected children are often treated with therapy regimens including protease inhibitors (PIs). We monitored the virol. response in a small group of pediatric patients undergoing therapy with regimens including the PI nelfinavir and determined whether new drug resistance mutations were present immediately after virol. failure. Seventeen reverse transcriptase inhibitor (RTI)-experienced children starting nelfinavir-containing therapy regimens were studied. After virol. failure, HIV-1 protease (PR) and RT sequences were examined for drug resistance mutations. Viral load levels decreased to <400 HIV RNA copies/mL in six patients and remained at <400 HIV RNA copies/mL in four patients. Three patients did not respond virol.; all three had mutations specific for one or more of their regimen drugs either before or soon after nelfinavir initiation. The virol. response was transient in eight patients whose viral loads did not decrease to <400 HIV RNA copies/mL. Genotypic data from seven of the eight patients revealed mutations specific for one or more of their regimen drugs after virol. rebound. PI resistance mutations occurred in eight patients: D30N in six, and L90M in three. In three patients, the only new mutation after failure was the RT mutation M184V. Despite virol. failure, sustained increases in CD4+ lymphocyte counts were noted in eight patients. We conclude that in this small group of pediatric patients, virol. failure occurred in all patients whose viral loads did not become undetectable after the switch to a nelfinavir-containing regimen. After failure, new drug resistance mutations were found in either PR or RT. Studies of larger cohorts are warranted to determine whether HIV-1 genotypic data can help in the formulation of effective salvage therapies in children.

IT 159989-64-7, Nelfinavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug resistance mutations in HIV-infected children taking nelfinavir-containing regimens)
RN 159989-64-7 CAPLUS
CN 3-Isoquinolinecarboxamide, N-(1,1-dimethylethyl)decahydro-2-[(2R,3R)-2-hydroxy-3-[(3-hydroxy-2-methylbenzoyl)amino]-4-(phenylthio)butyl]-, (3S,4aS,8aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FSTN INTERNATIONAL LOGOFF AT 11:29:17 ON 31 MAR 2008